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INTERPRETATION OF THE INTRAVENOUS CHOLANGIOGRAM

Robert E. Wise, M.D.
and
Richard G. O'Brien, M.D., Boston

• Sodium iodipamide injected intravenously was used in 300 cases in order to obtain serial cholangiograms. The results were studied in an effort to determine the various degrees of dilatation of the common bile duct, to relate them to preoperative and postoperative pain, and to establish criteria for preoperative diagnosis.

Neither the sulfobromophthalein retention test nor the serum bilirubin concentration afforded a basis for predicting whether the duct would be made visible by the sodium iodipamide. However, visualization never occurred when the serum bilirubin level was above 4.8 mg. or when the sulfobromophthalein retention was above 64%.

In 142 patients the bile passages were successfully visualized after cholecystectomy, so that the diameter of the common duct could be measured. These data were compared with the results of actually exploring the duct for obstructions. All ducts dilated to a diameter greater than 15 mm. were found to be partially obstructed, and all those narrower than 8 mm. were unobstructed. The 82 ducts of intermediate diameter (57% of the visualized cases) thus formed an important group in which the diameter of the duct was of no value in telling whether it was obstructed.

Sodium iodipamide intravenously visualized the gallbladder in 12 out of 34 patients in whom visualization when the medium was given orally had succeeded poorly or not at all.

A need has long existed for a safe, reliable, and accurate means of investigation of the status of the biliary ducts in addition to the indirect evidence afforded by certain laboratory procedures. The need has been especially great in evaluation of a patient who, after cholecystectomy, returns with the same or new symptoms referable to the biliary system. Great advancement in this direction has been made with the introduction of intravenous cholangiography using sodium iodipamide (Cholografin), the disodium salt of N,N′-adipyl-bis (3 amino-2, 4, 6-triiodobenzoic acid). Sodium iodipamide, in its present marketed state, a 20% solution, is identical to Biligrafin, originally employed in Germany for this procedure.[1] It has opened an entirely new field for investigation of the physiology and pathology of the biliary tract. Several preliminary reports have appeared in the United States.[2] However, problems of interpretation of these new studies have arisen. The visualization and interpretation of intraductal calculi are relatively simple and limited only by the relatively faint visualization of the bile ducts and by confusing overlying shadows.

Early in our experience it became apparent that there was marked variation in the diameter of postcholecystectomy common ducts. Although it has long been common knowledge that some dilatation of the common duct frequently takes place after cholecystectomy, our early experiences indicated that, at least in some instances, common bile ducts of only several millimeters in diameter could persist after cholecystectomy. Upon exploration, ducts with moderate degrees of dilatation in some instances were found to be completely unobstructed, and in other instances they were partially obstructed (fig. 1 and 2). Cattell and Colcock [3] have pre-

From the Department of Radiology, the Lahey Clinic. Dr. O'Brien is also a Trainee, National Cancer Institute.
Read before the Section on Gastroenterology and Proctology at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 8, 1955.

This study has been supported in part by the Squibb Institute for Medical Research.

1. Frommhold, W.: Ein neuartiges Kontrastmittel für die intravenöse Cholezystographie, Fortschr. Geb. Röntgenstrahlen **79**: 283-291 (Sept.) 1953. Gaebel, E., and Teschendoft, W.: Darstellung der Gallenwege mit Biligrafin (Schering): Unblutige Cholangiographie, Röntgen Blätter **6**: 162-170 (July) 1953. Hornykiewytsch, T., and Stender, H. S.: Intravenöse Cholangiographie, Fortschr. Geb. Röntgenstrahlen **79**: 292-309 (Sept.) 1953. Huber, K., and Stössel, H. U.: Die intravenöse Cholangiographie mit Biligrafin, Schweiz. med. Wchnschr. **84**: 117-118 (Jan. 16) 1954. Püschel, C.: Über klinische und röntgenologische Erfahrungen mit dem neuen I.v. Gallekontrastmittel Biligrafin, Deutsche med. Wchnschr. **78**: 1327-1329, 1953.

2. Bell, A. L. L., and others: Intravenous Cholangiography: A Preliminary Study, Am. J. Surg. **88**: 248-253 (Aug.) 1954. Berk, J. E.; Karnofsky, R. E. ; Shay, H., and Stauffer, H. M.: Intravenous Cholecystography and Cholangiography: Report of Preliminary Observations, Am. J. M. Sc. **227**: 361-371 (April) 1954. Berk, J. E.; Stauffer, H. M.; Shay, H., and Karnofsky, R. E.: The Normal and Abnormal Biliary Tract as Shown by Intravenous Cholecystography and Cholangiography, Gastroenterology **28**: 230-243 (Feb.) 1955. Fulton, H., and Sandweiss, D. J.: Intravenous Cholangiography: Preliminary Report, Harper Hosp. Bull. **12**: 106-111 (May-June) 1954. Glenn, F.; Evans, J.; Hill, M., and McClenahan, J.: Intravenous Cholangiography, Ann. Surg. **140**: 600-614 (Oct.) 1954. Orloff, T. L.; Sklaroff, D. M.; Cohn, E. M., and Gershon-Cohen, J.: Intravenous Choledochography with a New Contrast Medium, "Cholografin," Radiology **62**: 868-870 (June) 1954.

3. Cattell, R. B., and Colcock, B. P.: Fibrosis of the Sphincter of Oddi, Ann. Surg. **137**: 797-806 (June) 1953.

viously described similar findings in a review of 49 cases of surgically demonstrated fibrosis of the sphincter of Oddi, in only 17 of which an appreciable degree of dilatation of the common duct was found. This study was undertaken in an effort to determine the significance of the various degrees of dilatation of the common duct and to establish criteria for accurate preoperative diagnosis

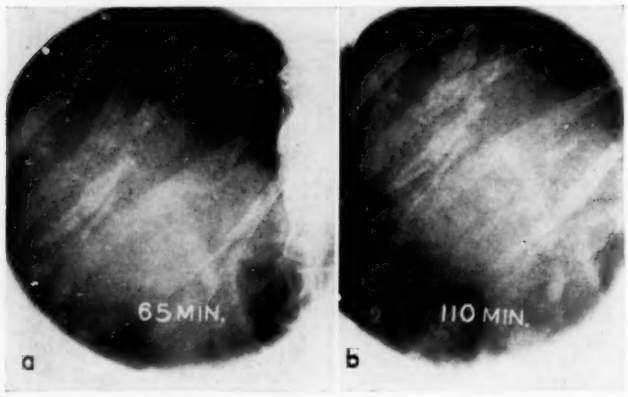

Fig. 1 (case 2, table 6).—Common duct, 10 mm. in diameter. *A*, at 65 minutes; *B*, at 110 minutes. Density of dye in *A* is equal to that in *B*. Gallbladder had not been removed, but it does not opacify presumably because of cystic duct obstruction (pathological cholecystectomy). Poor drainage is indicative of obstruction. Gangrenous gallbladder and cholelithiasis were found at operation. Obstruction was due to fibrosis of ampulla of Vater and sphincter of Oddi. Sphincterotomy was performed.

of the various degrees of obstruction of the common duct. Our preliminary observations have previously been recorded.[4] The present series comprises a total of 300 injections, including those previously reported. We now present additional data and conclusions.

Technique of Examination

Our technique of examination has previously been reported and does not differ greatly in its present form. The patient is examined usually in the morning in a fasting state after cleansing of the intestine with castor oil.

TABLE 1.—*Sulfobromophthalein Retention Recorded in 46 of 255 Visualized Cases**

Sulfobromophthalein Retention, %	No. of Cases	Sulfobromophthalein Retention, %	No. of Cases
0	6	16.0	2
Trace	2	20.0	3
2.0	8	21.0	1
4.0	5	22.0	1
6.0	5	28.0	1
8.0	1	32.0	2
10.0	1	56.0	1
12.0	3	64.0	1
14.0	3		

* 5.0 mg. per kilogram of body weight; 40-minute retention.

Except in a few instances, patients have been given 40 cc. of the 20% solution. In 30 instances, 20 cc. of a 40% solution (not yet available commercially) was used, and in these there was no significant difference in time or degree of opacification of the ducts. No apparent increase in rate or degree of side-effects was noted. The 40% solution appeared to present no advantage or disadvantage, other than greater convenience since a smaller quantity of the solution was injected. The patient is placed in the supine position with the left side elevated approximately 15 degrees. Films are made serially every 10 to 15 minutes throughout a period of at least two hours in the majority of cases. If the gallbladder is present and visualized, the examination is carried out longer, that is, to full opacification of the gallbladder. Each film is viewed immediately by the radiologist, and the various technical factors are adjusted as necessary.

Visualization

The types of cases in which injections were given and the number of visualizations obtained are as follows: In a total of 300 injections, visualization was obtained in 255 (85%). In 191 of these, in which cholecystectomy had been done previously, visualization was obtained in 158 (82.7%); in 109, in which cholecystectomy had not been done previously, visualization was obtained in 97 (88.8%). All patients examined were subjected to the procedure because of history, symptoms, or physical findings indicative or suggestive of disease of the biliary tract. No asymptomatic patients were examined. There is no significant difference in frequency of visualization before and after cholecystectomy. The figures relative to percentage of visualization are of value only in a broad sense, as they are based on a very highly selected group of cases.

As we have gained experience with respect to ability to predict whether visualization could be expected, the percentage of visualization has steadily increased. A desire to improve this accuracy has prompted us to analyze the various liver function tests and their relation to duct visualization. Serum bilirubin and sulfobromophthalein (Bromsulphalein) sodium retention studies appeared the most likely to be of significant value in predicting visualization. Accordingly, these laboratory studies of the 300 patients were reviewed.

Fig. 2 (case 1, table 6).—Common duct, 9 mm. in diameter. *A*, 60 minutes after injection. Note slightly blunted hepatic radicles and relatively parallel margins of common duct, both suggestive of obstruction. There is abrupt blunt ending at distal end of common duct. *B*, 120 minutes after injection. Density of dye in common duct is slightly greater than at 60 minutes. At operation, an obstructing calculus was found in common duct.

In the 255 instances in which visualization was obtained, the sulfobromophthalein retention was recorded in 46. These are listed in table 1. The serum bilirubin

4. Wise, R. E., and O'Brien, R. G.: (*a*) Intravenous Cholangiography: A Preliminary Report, Lahey Clin. Bull. **9**: 52-56 (Oct.) 1954; (*b*) Symposium on Surgery of the Digestive Tract: Intravenous Cholangiography, S. Clin. North America **35**: 755-763 (June) 1955.

values were recorded in 81 of the 255 cases, and these are given in table 2. Thus it is seen that visualization was obtained with sulfobromophthalein retention as high as 64% in one instance and with a serum bilirubin level as high as 4.8 mg. in another. Sulfobromophthalein retention and serum bilirubin values in the nonvisualized cases are tabulated in tables 3 and 4. It will be noted

TABLE 2.—*Serum Bilirubin Level Recorded in 81 of 255 Visualized Cases*

Serum Bilirubin, Mg.	No. of Cases	Serum Bilirubin, Mg.	No. of Cases
Trace	3	1.0	1
0.1	12	1.1	4
0.2	11	1.2	4
0.3	6	1.4	1
0.4	8	1.8	1
0.5	6	1.9	1
0.6	2	2.7	1
0.7	8	2.8	2
0.8	4	4.8	1
0.9	5		

from these that in one instance visualization was not obtained with a sulfobromophthalein retention of only 6% and a serum bilirubin value of only 0.1 mg. It is apparent from an examination of these four tables that a considerable spread exists in both tests with respect to visualization. There appears to be no sharp line of demarcation in either procedure where the probability of visualization can be predicted with absolute accuracy. It appears, however, that there is relatively little use in attempting the study in those patients with a serum bilirubin value above 4.0 mg. and in those with a sulfobromophthalein retention above 40%.

Reactions

Reactions of varying degree have been recorded in 34, or 11.3%, of the 300 injections. Of the 34 patients who had reactions, skin tests (0.1 cc. of full-strength solution given intracutaneously) were recorded in 28 instances. Of these, 17 tests were regarded as negative and 11 as positive. An additional 94 skin tests were recorded in those patients who did not have reactions, and, in these, 13 were regarded as positive and 81 as negative. This suggests that there is an increase in incidence of

TABLE 3.—*Sulfobromophthalein Retention Recorded in Eighteen of Forty-Seven Nonvisualized Cases*

Sulfobromophthalein Retention, %	No. of Cases	Sulfobromophthalein Retention, %	No. of Cases
6.0	1	44.0	1
14.0	1	48.0	2
16.0	1	52.0	1
24.0	1	64.0	1
32.0	1	66.0	1
36.0	3	72.0	2
40.0	1	84.0	1

reaction in those with positive skin tests, but inspection of the figures indicates that the line of demarcation between the reactors and nonreactors is not sharp enough to place much reliance upon it, nor has the skin test been of any significance in predicting the severity of reaction. It would appear from the above that there is very serious question as to whether the skin test is of any value, and it is our opinion that it is of no practical value.

The above figure of 11.3% reactions is somewhat at variance with our previously published rate of 20%, which was based on only 116 cases.[4b] There are at least two reasons for this. The first is that a number of our earlier findings were the result of suggestion; the second is the difference in recording reactions. In the first series, the patients were quizzed at great length about reaction, but at present the tendency is to record only those reactions of which the patient complains.

To date there have been no serious reactions; the various types encountered were as follows: vasomotor collapse, one; nausea, 12; pruritus, 2; nausea and vomiting, 8; dizziness, one; sneezing, 2; urticaria, 2; chills, 3; faintness, one; bronchospasm, one; and erythema, one. It is our present practice to administer 20 mg. of diphenhydramine (Benadryl) hydrochloride intravenously before the dye is injected and then to inject 1 cc. of the dye intravenously and wait one to two minutes before injecting the full amount. If there is no reaction to the 1-cc. intravenously given test dose, the full amount is injected. It is our impression that premedication with diphenhydramine tends to reduce the incidence and degree of nausea and vomiting. All patients are quizzed regarding possible allergies. If a strong allergic background is present, the examination is deferred and antihistaminic substances are given orally for two days prior to injection.

TABLE 4.—*Serum Bilirubin Level Recorded in Twenty-Nine of Forty-Seven Nonvisualized Cases*

Serum Bilirubin, Mg.	No. of Cases	Serum Bilirubin, Mg.	No. of Cases
0.1	4	3.3	1
0.2	1	4.4	1
0.6	1	4.9	1
1.1	1	5.2	3
1.2	2	5.3	1
1.3	1	6.2	1
1.7	1	7.6	1
1.8	1	8.9	1
2.5	1	10.0	1
2.6	2	12.6	1
3.2	1	18.8	1

Size of Common Ducts

A review of 142 of the visualized postcholecystectomy cases indicated a wide range in diameter of the common duct (fig. 3). They varied from a minimum of 3 mm. in four instances to a maximum of 30 mm. in one instance. The greatest number (29) were found to measure approximately 10 mm. in diameter. Since there is such an unusual discrepancy between the number of ducts measured as 9, 10, and 11 mm., possibly the discrepancy is due to a tendency to record the size in "round numbers." The values given are the actual measurements on the films and represent a magnification of approximately 30%, which varies somewhat with the size of the patient and the degree of rotation.

In an attempt to determine the significance of size, the operative cases in which the common duct was either explored or visualized adequately enough to enable the operator to estimate its condition were reviewed. Two groups were analyzed: those showing evidence of obstruction of the distal end of the ducts and those without obstruction. The first group comprised 36 cases in which

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the ducts were explored and visualized. This figure excludes the fistulas and cases in which the common duct was not visualized because of findings such as malignancy. The second or unobstructed group included 32 cases that met the conditions described above. Comparison of the two groups showed that the unobstructed ducts varied from 3 to 15 mm. in diameter and the obstructed group, from 8 to 30 mm. (fig. 3).

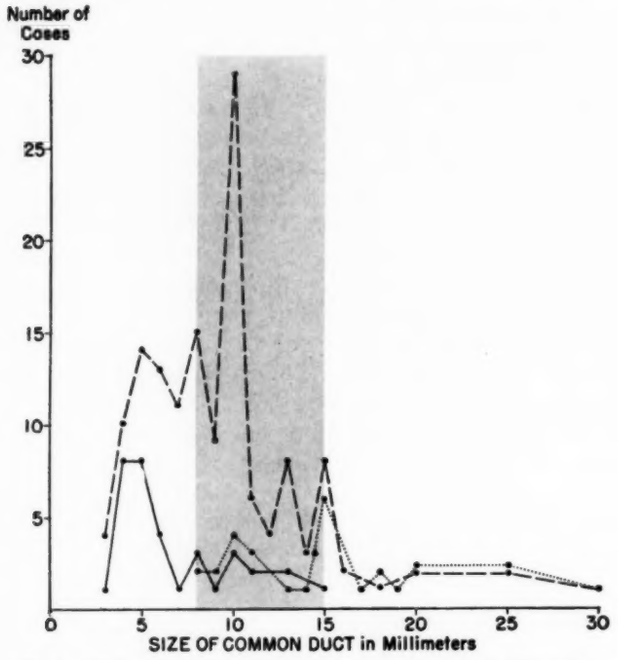

Fig. 3.—Size of common ducts in all postcholecystectomy cases, in proved cases of partial obstruction and proved cases without obstruction. Broken line, all postcholecystectomy cases (142); dotted line, proved cases with partial obstruction (36); and solid line, proved cases without obstruction (32).

In figure 3 the curves of common duct size in millimeters are plotted against numbers of cases for (1) all visualized postcholecystectomy common ducts that could be measured, (2) proved cases of unobstructed common ducts, and (3) proved cases of common ducts with partial obstruction. It is evident from these curves that there is one area, from 8 to 15 mm., where curves for obstructed and nonobstructed common ducts markedly overlap. Above 15 mm. all explored common ducts have been shown to be partially obstructed, and below 8 mm. all explored common ducts have been unobstructed. It is apparent from this figure that only at extreme ends of the scale, that is, from 3 to approximately 8 mm. and from 15 to approximately 30 mm., the size of the common duct alone is significant in determining the presence or absence of obstruction. In the midportion (shaded area), from 8 to 15 mm., size apparently is of no value except to indicate that partial obstruction may possibly be present. Tabulation of the total number of cases with ducts measuring between 8 and 15 mm. shows that 82 out of a total of 142 visualized postcholecystectomy common ducts fall in this group. Thus it is apparent that, in at least 57% of the cases, the size of the common duct is of no value in determining the presence or absence of obstruction.

Criteria other than merely size of the common duct were necessary if we were to analyze accurately the status of the biliary tract in the postcholecystectomy case. It had been noted early in our studies that there was considerable variation in the length of time the ducts remained opacified. The undilated ducts, that is, those measuring 3 to 4 mm. in size, frequently were empty 60 and 90 minutes after injection. The larger ducts frequently remained opacified for two hours or more. A number of these were explored for various reasons, such as predicted obstruction on the basis of abnormal retention of dye, question of disease in the pancreas, or question of calculi in the common duct or cystic duct remnant, thus allowing us the opportunity to review surgically proved findings. It was further noted that, if the gallbladder was present and visualized with sodium iodipamide, the ducts usually remained opacified for periods of time much longer than two hours. In those cases, however, in which the gallbladder was not visualized with sodium iodipamide because of cystic duct obstruction, the common duct behaved in much the same manner as the postcholecystectomy ducts, that is, the size and emptying time were variable. For study purposes it appeared logical to add these two groups together. All cases in which the gallbladder was visualized, a fistula was present, visualization was too poor for measurement, or morphine had been administered were excluded. Cases in which the gallbladder filled were excluded since it had already been determined that in these cases there was no relationship between the retention of dye in the duct and the patency of the common duct.

A total of 38 cases meeting the conditions above, of which 23 were proved to have partial obstruction and 15 no evidence of obstruction, was then available for study. The films of these two groups were reviewed and the density of the dye was graded on a one to four plus basis at 15-minute increments from 0 to 120 minutes. The unobstructed cases are shown in table 5 and the partially obstructed cases in table 6. Composite curves were then obtained by taking the average density at each 15-minute interval and plotting this against the time interval after injection over a 120-minute period. Figure 4 shows the curves with the solid line representing the proved unobstructed cases and the dotted line representing the proved partially obstructed cases. A significant difference in the two curves is noted with respect to time of retention of dye in the common duct. It is apparent in the unobstructed cases that there is a very rapid decrease in

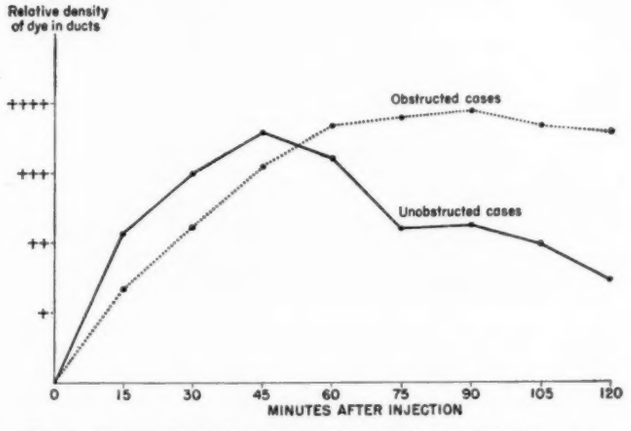

Fig. 4.—Curves illustrating relative dye densities and drainage rates of unobstructed versus obstructed ducts.

density after 45 minutes. In many of the unobstructed cases the ducts are completely empty at 120 minutes as shown in table 5, but the composite curve indicates a relative density of 1.4 at 120 minutes and the curve of the obstructed cases, a relative density of 3.6 at 120 minutes. It is upon this that we now base our estimation of the presence or absence of obstruction; that is, for a diagnosis of partial obstruction of the distal end of the common duct, the density of the dye in the duct at 120 minutes must be not significantly less than the density

TABLE 5.—*Relative Density of Dye in Surgically Proved Unobstructed Common Ducts*

Case	Minutes After Injection								Size of Common Duct, Mm.	Surgical Findings
	15	30	45	60	75	90	105	120		
1	+++	++++	.....	.....	++	.....	.....	+	7	Common duct visualized; not explored; considered normal
2	+	++	+++	++++	+++	.....	+++	++	9	Chronic pancreatitis; no. 6 Bakes dilators passed sphincter
3	++	++++	++++	.....	++	.....	.....	+	6	Cholecystitis; impacted cystic duct stone; common duct normal; not explored
4	++	.....	.....	++++	+	.....	.....	.....	5	Cholecystitis; impacted cystic duct stone; common duct normal; not explored
5	.....	++	++++	.....	+++	.....	+++	++	8	Laparotomy; common duct visualized and considered normal; not explored
6	++++	+++	+++	.....	.....	+	.....	.....	4	Cystic duct remnant; common duct visualized and considered normal
7	++++	++++	+++	++	.....	0	0	.....	5	Cystic duct remnant with calculus; common duct explored; no. 6 Bakes dilator passed
8	+++	++++	.....	+++	.....	+++	.....	++	8	Contracted gallbladder; chronic cholecystitis; common duct slightly dilated; not explored
9	++	++++	.....	+++	.....	+++	.....	++	4	Cystic duct remnant with calculi; common duct normal; explored
10	++	++++	.....	+++	++	++	.....	0	4	Cholecystitis and cholelithiasis; common duct appeared normal; not explored
11	+	++	.....	+++	.....	++++	.....	++	13	Thickened common duct wall; no. 6 Bakes dilator passed easily
12	++	++++	++++	+++	.....	++	.....	.....	10	Chronic pancreatitis; no. 7 Bakes dilator passed with ease
13	+	++	++++	+++	.....	+++	.....	.....	5	Cystic duct remnant; common duct explored; normal
14	++	+++	++++	.....	+	.....	.....	.....	6	Common duct explored; Bakes no. 8 dilator passed with ease
15	+	++	+++	++++	++++	+++	++	.....	10	Common duct not explored; considered normal at surgery
Average density of dye	2.1	3.0	3.6	3.2	2.2	2.3	2.0	1.5		
Average size of common duct.....									6.9 mm.	

TABLE 6.—*Relative Density of Dye in Surgically Proved Partially Obstructed Common Ducts*

Case	Minutes After Injection								Size of Common Duct, Mm.	Surgical Findings
	15	30	45	60	75	90	105	120		
1	++	+++	++++	++++	++++	++++	++++	++++	9	Common duct calculus; no fibrosis
2	+	+	++	++++	.....	.....	.....	++++	10	Fibrosis of ampulla of Vater and sphincter of Oddi; sphincterotomy
3	+	++	+++	++++	++++	++++	.....	++++	11	Stenosis of sphincter of Oddi; cystic duct remnant with calculi
4	+	++	++++	++++	++++	++++	.....	.....	17	Calculus at ampulla of Vater
5	+	++	++	+++	++++	++++	++++	.....	12	Stricture of ampulla of Vater and fibrosis of sphincter of Oddi; manual dilatation up to no. 9 Bakes
6	0	+	++	++++	++++	++++	.....	++++	9	Sphincter dilated with difficulty; possible fibrosis of sphincter of Oddi; sphincterotomy done
7	+++	++++	.....	++++	++++	.....	++++	++++	14	Sphincter dilated with difficulty only to no. 5 Bakes; sphincterotomy done; fibrosis of ampulla of Vater
8	.....	+	.....	++++	++++	.....	.....	++++	18	Sphincter of Oddi stenosed; passed only 1 mm. probe; two 1 mm. calculi; sphincterotomy
9	+	.....	+++	++++	.....	++++	.....	++++	13	Fibrosis and inflammation of ampulla of Vater; sphincterotomy
10	+	++	+++	+++	.....	++++	.....	++++	25	Common duct calculi
11	+	+	.....	++++	++++	++++	.....	++++	10	Several common duct calculi; sphincter of Oddi normal
12	++	++	+++	+++	.....	++++	.....	++++	15	Sphincter of Oddi stenosed, could not be probed; sphincterotomy; several small common duct calculi
13	+++	.....	.....	++++	.....	++++	.....	++++	8	Sphincter of Oddi "tight"; manually dilated to no. 7 Bakes
14	+	+++	++++	++++	.....	++++	++++	.....	10	Common duct calculus; no. 5 Bakes passed; stricture of ampulla of Vater; sphincterotomy
15	++	+++	++++	++++	.....	++++	.....	.....	12	Carcinoma of head of pancreas 4 to 5 cm. in diameter
16	.....	.....	+++	++++	.....	++++	.....	++++	20	Carcinoma of ampulla of Vater
17	+	++++	++++	+++	.....	++++	.....	+++	30	Several large soft stones; sphincterotomy
18	.....	+	+++	++++	.....	.....	.....	++++	18	Narrowing of ampulla of Vater; sphincterotomy
19	+	++	+++	++++	.....	++++	.....	++++	19	Common duct calculus 1.5 cm. in diameter
20	.....	++	+++	++++	++++	++++	.....	++++	11	Common duct calculus; slight fibrosis of sphincter of Oddi
21	0	++	+++	+++	+++	+++	.....	++++	25	Three large common duct calculi
22	+	.....	+++	+++	+++	++++	.....	++++	15	One 8 mm. common duct calculus; ampulla narrow; no. 8 Bakes passed; sphincterotomy
23	++	+++	+++	+++	++++	++++	++++	.....	18	Sphincter tight admitting no. 3 Bakes; manual dilatation up to no. 8 Bakes; long-arm T-tube inserted
24	Not timed on films								8	Fibrosis of sphincter of Oddi; could not be probed; sphincterotomy
Average density of dye	1.3	2.2	3.1	3.7	3.8	3.9	3.7	3.8		
Average size of common duct.....									14	

at 60 minutes. If the density of dye at 120 minutes is significantly less than it was at any time prior to 120 minutes, we now believe that there is no evidence of significant obstruction of the duct. We cannot be certain that minimal degrees of obstruction do not exist in some moderately dilated ducts that empty somewhat more rapidly than indicated in the "obstructed curve," but we do not at the present time have evidence to suggest that they are of significance.

Presence of visible dye in the duodenum does not exclude the possibility of partial obstruction of the common duct. If the common duct were not partially patent, a marked degree of obstructive jaundice would be present and no visualization would be obtained. Therefore, some dye in the duodenum is to be expected in almost all cases. The greater the degree of obstruction, the less dye one will see in the duodenum, as a general rule, but in several instances of stricture and of very marked fibrosis of the sphincter of Oddi we have seen considerable dye in the duodenum. Concentration of dye in the duodenum is dependent on two factors. The first is the degree of patency of the sphincter of Oddi and the second is duodenal activity.

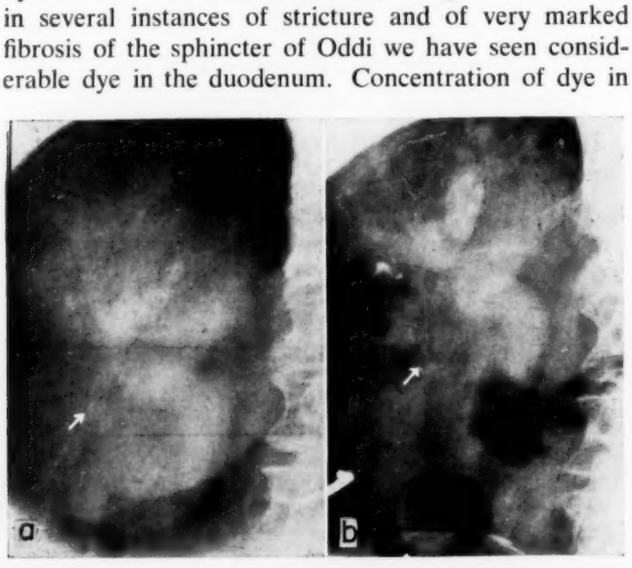

Fig. 5 (case 18, table 6).—Cholecystostomy had been performed 30 years previously. There was no visualization of gallbladder with sodium iodipamide due to obstruction of cystic duct by calculi, as shown at arrows. This represents pathological cholecystectomy. *A*, 60-minute film showing obstructing calculi in cystic duct and dilated common duct (18 mm.); *B*, 135-minute film after inhalation of amyl nitrite (no visible effect), showing abnormal retention of dye indicative of partial obstruction of distal end of common duct. At operation, gallbladder was small and contracted and contained several calculi. Common duct was dilated and ampulla of Vater was narrowed. Sphincterotomy was performed.

In all instances in which the gallbladder has filled to any degree, it was noted that the above time-density relationship did not hold. Although it has been shown that some dilatation of the common duct may exist in the absence of obstruction, it appears that the postcholecystectomy bile ducts are essentially semirigid tubes through which the bile is forced by the pressure created by the constant secretion of bile from the liver. We have seen no evidence that the sphincter of Oddi alternately contracts and relaxes, but rather it is our impression that a constant degree of patency is maintained by the intraductal pressure above. However, if the gallbladder is present and the cystic duct is not obstructed, the constant pressure that maintains patency of the sphincter of Oddi apparently is reduced by filling of the expansile gallbladder. The sphincter then either contracts or the intraductal pressure is not sufficient to clear the duct of sodium-iodipamide-stained bile, but in either event the common duct remains opacified for an unusually long time and the time-density factors described above do not hold in the presence of a gallbladder that shows any degree of filling. If the cystic duct is obstructed by calculi or inflammation, however, we then have, in effect, a pathological cholecystectomy and the physiology and dynamics are essentially the same as in a postcholecystectomy common duct (fig. 5). Examination of the curves in figure 4 indicates that maximum density of the dye is obtained slightly earlier in the unobstructed cases, and it is also apparent that maximum dye density is slightly greater in the obstructed cases.

Common Duct Calculi

In 14 cases the presence of common duct calculi was proved at operation. In 6 of the 14, there was an associated fibrosis of the sphincter of Oddi or the ampulla of Vater, and in one there was an associated stricture of the common duct. In only 7 of the 14 were the calculi actually visualized prior to operation. In the remaining seven, however, partial obstruction of the common duct was noted and these seven patients were operated on. In three of these cases in which the diagnosis was made by the presence of obstruction, there was no evidence of associated fibrosis of the sphincter of Oddi or the ampulla of Vater (fig. 2).

Although it is obviously better actually to visualize the calculi if possible, it is apparent from the above that this is not necessary. It is more important to decide whether or not obstruction is present. The obstructive factor, whether it be due primarily to the calculi or to an associated fibrosis if this be present, is the true indication for surgery rather than the mere presence of calculi. Possibly, planigraphic examination of those cases in which the calculi were not visualized might have demonstrated some of them. We have not used this modality but instead have relied upon the obstructive factor for diagnosis.

Common Bile Duct Strictures

The vast majority of patients with common bile duct strictures seen at this clinic are not good candidates for intravenous cholangiography because of the severe liver damage of jaundice usually present. However, in this series, five strictures were visualized. In one instance, visualization was relatively poor and only the proximal portion of the stricture was visualized, but in the remaining four good visualization was obtained and in each instance a marked differential in size was noted proximal and distal to the stricture (fig. 6). In each instance the diameter of the proximal portion measured approximately twice that of the distal portion. In several instances, considerable dye was visible in the duodenum, but it is true in considering strictures, as it is in considering obstructions of the distal end of the duct, that, since the obstruction is not complete, we can expect a certain amount of dye to be visible in the duodenum and also in the distal or unobstructed portion of the common duct,

since there is continual, slow seepage past the stricture resulting in continuous visualization of the distal portion. For this reason we cannot expect to find a marked difference in emptying time between the portions of the duct distal and proximal to the stricture.

Although the test has proved useful in only a small percentage of the patients with strictures seen and operated on at this institution, it still is of considerable value, since it is in the equivocal cases, which may well be missed clinically, that it is most needed. In the majority of common duct strictures the diagnosis can be made on clinical grounds.

Laboratory Studies in Obstructed Cases

The serum bilirubin value was recorded in six cases of partial obstruction of the common duct as follows: narrowing of ampulla (sphincterotomy), 0.1 mg. per 100 cc.; carcinoma, head of pancreas, 0.2; stricture of common duct, 0.4; carcinoma, ampulla of Vater, 0.4; common duct calculi, 0.8; and fibrosis, sphincter of Oddi, 1.4. The sulfobromophthalein retention was recorded in seven

TABLE 7.—*Sulfobromophthalein Retention in Partial Obstruction as Recorded in Seven Cases*

Diagnosis	Sulfobromophthalein Retention, %
Fibrosis, sphincter of Oddi (sphincterotomy)	0.0
Fibrosis, ampulla of Vater (sphincterotomy)	2.0
Sphincter "tight" (sphincter dilated manually)	6.0
Carcinoma, head of pancreas	10.0
Narrowing of ampulla (sphincterotomy)	12.0
Common duct calculus	14.0
Fibrosis, sphincter of Oddi and ampulla of Vater (sphincterotomy)	28.0

cases (table 7). Serum alkaline phosphatase values in Bodansky units were as follows: visualized cases, 1.1 to 21.1; nonvisualized cases, 3.5 to 29.4; and visualized cases with partial obstruction, 1.9 to 15.1.

It would appear from these results that in none of these laboratory procedures is there an accurate level above or below which one may safely predict or exclude partial obstruction. Although it is true that there was a significant rise in some cases with the three procedures, it is apparent that the presence of partial obstruction cannot safely be excluded on the basis of laboratory studies alone.

Morphology of the Biliary Ducts

Although common duct size and length of time the dye is retained in the ducts are of great diagnostic significance, there are other factors that we have observed and that we believe are of considerable significance. The obstructed duct is usually slightly more tortuous than the unobstructed, and the hepatic radicles, when visualized, appear to be slightly blunted. The length of the common duct should be observed carefully, as this in itself is of considerable significance since many strictures are at the level of the cystic duct or higher. Also, of course, calculi may be lodged at any level of the duct. Therefore, if a duct appears shorter than usual, obstruction should be suspected.

Although size is of significance and our measurements, as given throughout this paper, represent the widest point of the duct, it is apparent upon reviewing the obstructed cases that these common ducts are usually of a uniform width, at least in the distal two-thirds or three-fourths. We have observed a number of ducts in which the widest point was considerably greater than the diameter at the distal end of the common duct. One such proved instance was found in which the widest point of the duct was 13 mm., but it tapered gradually to several millimeters at the distal end. This duct was proved to be normal and unobstructed at operation. This is one instance in which a rather large duct was seen to retain dye in high concentration for more than two hours. Early in our experience we considered this evidence of obstruction, but there is one important factor that we would consider today in evaluating a situation of this type. The gallbladder is present and visualized, and this accounts for the dye retention in the duct.

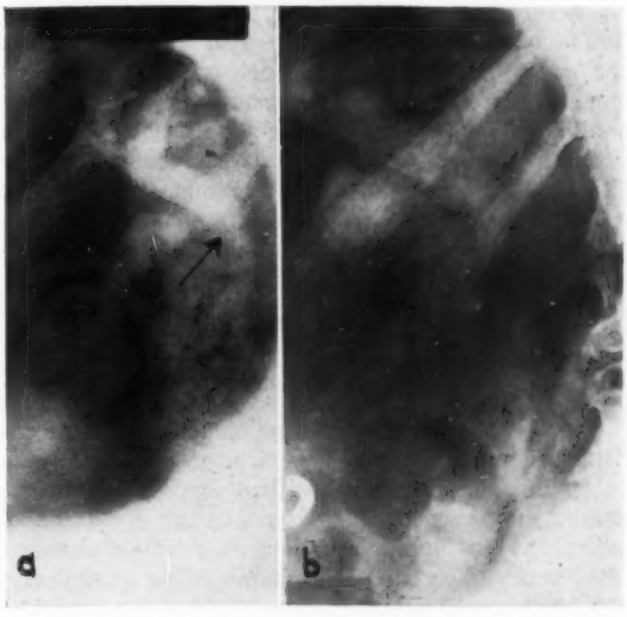

Fig. 6.—*A*, postcholecystectomy common duct (60 minutes). Thin linear defect across duct is visible at level of arrow. The duct measures 15 mm. above and 7 mm. below the arrow. In view of difference in size of proximal and distal duct and marked retention of dye at 120 minutes, *B*, diagnosis of stricture of common duct was made. Stricture that admitted only small probe was found at operation.

Effect of Drugs

In several instances morphine was administered and in each instance the sphincter of Oddi was apparently closed and the density of dye in the ducts was increased, resulting in better visualization of the ducts. However, it has not been our practice to use it, since it completely eliminates or destroys the concept of the time-density relationship, as outlined in the foregoing parts of this communication, by creating a pharmacological obstruction. Amyl nitrite was administered in several instances, without effect. Only one of these patients has been operated on, and this patient was one in whom an 18 mm. common duct was noted without significant dye in the duodenum. Amyl nitrite was given and there was no detectable change in rate of emptying of the common duct. At operation, narrowing of the ampulla of Vater was found and a sphincterotomy was done (fig. 5).

Nonvisualization of Gallbladder with Oral Cholecystography

Thirty-four patients in whom visualization of the gallbladder by the oral method was either very poor or absent received injections of sodium iodipamide. In 12 of these cases the gallbladder was visualized with sodium iodipamide. In eight, calculi were visualized in the gallbladder, and in four instances the gallbladder appeared normal. In 22 of the 34 cases, the gallbladder was not visualized on the intravenous cholangiogram but there was good visualization of the ducts. Twelve of these patients have been operated on. Ten showed obstruction of the cystic duct. One patient had a cholecystojejunal fistula, and in another a carcinoma of the head of the pancreas was present. Ten of the patients have not as yet been operated on.

In one instance in which the gallbladder was not visualized, even though adequate dye was visible in the biliary ducts, a roentgenogram of the kidney, ureter, and bladder made the following day showed excellent visualization of the gallbladder. It would appear from the above that the intravenous cholangiogram is considerably more accurate than oral cholecystography in predicting nonfunctioning gallbladder. If a good quantity of dye is visible in the biliary ducts and the gallbladder does not visualize, this very likely is evidence that the cystic duct is obstructed, preventing filling of the gallbladder. However, in view of the isolated instance in which the gallbladder was visualized 24 hours after injection of sodium iodipamide, we now attempt to make a 24-hour film on all such patients.

Cystic Duct and Gallbladder Remnants

Cystic duct remnants and gallbladder remnants are visualized quite regularly. This ability to visualize cystic duct remnants affords an excellent opportunity to determine the presence or absence of calculi in cystic duct remnants. Usually our task consists chiefly in deciding whether or not certain calcifications visible on the plain film of the right upper abdominal quadrant represent calculi, but in one instance a nonopaque calculus was found. We have visualized and have had surgical verification in six instances. In one case calcifications had formed about the sutures surrounding the cystic duct, and these were misinterpreted as calculi in a cystic duct remnant.

Sources of Error

Several potential sources of error have been noted. The first of these is the pyelogram, which is obtained usually at 10 minutes. This should not be confusing so long as one is aware of its occurrence. The radiologist must be careful not to interpret the dye-filled duodenal bulb as a gallbladder. In one instance, considerable dye apparently passed into the gastric antrum, simulating a gallbladder. In one case, a 15 mm. common duct was found that retained dye in very heavy concentration for over two hours. It was thought that this probably indicated obstruction of the common duct. The gallbladder had not been removed but did not visualize with sodium iodipamide. At surgical exploration, a cholecystoduodenal fistula was found. This is another instance in which the drainage factor, as shown in figure 4, does not hold true. The mechanism is apparently much the same as the mechanism of long retention of dye in the duct in the presence of a visualized gallbladder, that is, the unobstructed cystic duct relieves the pressure on the sphincter of Oddi, allowing it to remain closed and thus retain the dye in the common duct. In this instance the fistula relieves the pressure on the sphincter of Oddi, permitting dye to remain in the duct.

Cholecystography

Cholecystography with sodium iodipamide presents several problems. Although visualization of the gallbladder is very rapid, considerable layering occurs. It is readily apparent that, if calculi were to layer in the unstained portion of the bile, they would remain undetected. We have found considerable variation in the length of time necessary to obtain homogenous opacification of the gallbladder. It is our opinion that cholecystography with sodium iodipamide is unsafe unless decubitus or upright films are made, and the examination cannot be considered complete until homogenous opacification is complete.

Comment

The technique of intravenous cholangiography is not difficult but demands the personal attention of the radiologist to insure optimal accuracy. It does not appear that in the foreseeable future the examination can be placed on a routine basis such as is common practice with intravenous pyelography. The efficiency and accuracy of the examination are dependent to a great degree upon the diligence and care of the radiologist. It is true that one of the limitations to the procedure is the significant percentage of nonvisualization in patients with jaundice and liver damage, as indicated above. This is a serious limitation, but, fortunately, it is true that in a great many of these cases the diagnosis can be made on clinical grounds alone. It is in the cases in which diagnosis cannot be made on clinical grounds that the greatest value lies. These patients frequently are those with distressing symptoms and without definite laboratory evidence of common duct disease. McDonough and Wise,[5] in a clinical evaluation of the test, indicate that, in 18% of cases in which visualization was obtained, the intravenous cholangiogram alone was responsible for establishing the diagnosis. This represents a substantial increase in diagnostic accuracy. Although the side-effects occur rather frequently, they have not been serious nor do they represent a serious drawback to the procedure.

Laboratory studies are of value only as a rough guide in prediction of visualization. There are several instances of visualization with extremely high sulfobromophthalein retention and serum bilirubin values and several instances of nonvisualization with very low values that we cannot explain. Our percentage of visualization could undoubtedly be increased by closer attention to the laboratory studies before considering the examination. The economics of medicine, however, dictate that we cannot always wait for these studies before proceeding with

5. McDonough, F. E., and Wise, R. E.: Limitations to the Clinical Application of Intravenous Cholangiography in Determining Disease of the Bile Ducts After Cholecystectomy, Gastroenterology **29**: 771-788 (Nov.) 1955.

the examination. It is apparent from studying the laboratory results presented and the results of McDonough and Wise [5] that a diagnosis of common duct disease cannot be made from laboratory studies and clinical evaluation alone in a significant number of cases.

Although we do not believe that morphine should be used routinely with the procedure because it nullifies the time-density factor, we do believe that it has a very definite place in intravenous cholangiography when used judiciously. We have found no evidence that amyl nitrite is of value in relaxing the sphincter of Oddi. There is, however, considerable room for further investigation of various pharmacological agents upon the sphincter. The procedure should not be used for routine cholecystography because of the slight but real hazard that accompanies any intravenous injection. However, the procedure is indicated after failure of visualization of the gallbladder with orally given dye, since, as shown above, a significant number of gallbladders that did not visualize with orally given dye did so with intravenously administered dye. It is in these cases, also, that we expect the procedure to be of value for preoperative evaluation of the common duct relative to calculi and partial obstruction.

Although the most obvious use of this procedure is in the visualization of common duct calculi, it became apparent quite early in our experience that determination of the presence or absence of partial obstruction of the common duct was of considerably more importance. This is borne out by the fact that in only 50% of the cases of common duct calculi were they actually demonstrated by the cholangiogram. The experience of Cattell and Colcock, in a review of 49 cases of fibrosis of the sphincter of Oddi, indicated the importance of the obstructive factor in evaluation of the common duct. In their patients, diagnosis (at operation) and definitive treatment resulted in complete relief of symptoms in 90%.

It is the obstruction to the free flow of bile through the common duct, whether the obstruction be due to calculus, stricture, fibrosis of the sphincter of Oddi, or other cause, that usually is responsible for the symptoms. The determination of this obstruction constitutes the most valuable application of intravenous cholangiography. Surgically proved cases showing partial obstruction were as follows: fibrosis of sphincter of Oddi and ampulla of Vater, 10; common duct calculi, 7; fibrosis of sphincter of Oddi plus calculi, 6; common duct strictures, 3; hepatic duct strictures, 2; carcinoma of pancreas, one; carcinoma of common duct, one; carcinoma of ampulla of Vater, one; and stricture of common duct plus calculi, one.

It would, therefore, appear that the most important decision to be made is whether or not partial obstruction exists. Size has been shown to be of only limited value in prediction of partial obstruction. This is in agreement with the experience of Cattell and Colcock, who found an appreciable degree of dilatation in only 17 of 49 cases. Morphology of the ducts, likewise, is of limited value. The time-density relationship, as already outlined, appears to be the most valuable method of estimating the degree of patency of the common duct.

The figures in table 5 and the curves of figure 4 suggest a normal clearance rate of sodium iodipamide by the liver over and above the excretion by the kidneys. Preliminary observations suggest that in the majority of cases almost all of the sodium iodipamide should have been cleared from the blood stream within 120 minutes.

The very marked difference in emptying rate of the common duct between those patients with intact functioning gallbladders and postcholecystectomy patients suggests a fundamental difference in the state of the sphincter of Oddi. In the postcholecystectomy or pathological cholecystectomy cases, the sphincter of Oddi becomes relatively functionless and permits constant drainage of the common duct because of the pressure exerted by the excretion of bile by the liver. If a partial obstruction of the distal end of the common duct exists, there is an associated dilatation of the common duct of varying degree. If the gallbladder is present and the cystic duct is not obstructed, the sphincter of Oddi apparently remains contracted most of the time and the expansile gallbladder functions to relieve pressure on the sphincter of Oddi, permitting it to remain closed and retain dye in the common duct for an indefinite period of time.

Summary and Conclusions

Intravenous cholangiography is a relatively safe procedure that is indicated in evaluation of the patient with the same or new symptoms referable to the biliary tract after cholecystectomy. It is not indicated as a substitute for oral cholecystography but is indicated in those patients in whom the gallbladder fails to visualize with orally given dye, in order to evaluate more accurately the status of the gallbladder and the common duct as well. Partial obstruction of the common duct appears to be relatively common in the "postcholecystectomy syndrome" group of patients. Proper precholecystectomy use for evaluation of the common duct should result in fewer failures of gallbladder surgery. We believe that this procedure may necessitate reevaluation of some of our concepts of the postcholecystectomy syndrome. More widespread use and further knowledge will lead to a more accurate evaluation of the postcholecystectomy syndrome. The disease in a significant number of these patients will be removed from a functional classification to a classification of organic disease, and the prospect of cure with definitive surgery will be improved.

605 Commonwealth Ave. (15) (Dr. Wise).

Disposal of Radioactive Wastes.—The disposal of radioactive wastes may well prove to be one of the limiting factors in achieving optimum benefits from the general usage of nuclear energy. In the program of radiation protection, environmental exposures are most important and control of the environment is the most fruitful field of endeavor. During the present period of expansion the sanitary engineer has an opportunity and a challenge to prepare himself and to draw upon his previous experiences in helping to find rational solutions to the problems of radioactive wastes. He must gain an acquaintance with the principles of nuclear phenomena and with the technics of radiation monitoring and control. With regard to ground disposal of radioactive wastes, the sanitary engineer should arrive at decisions based upon an understanding of the hazards and a thorough knowledge of the scientific bases for particular proposals.—R. J. Morton, C.E., and E. G. Struxness, Ground Disposal of Radioactive Wastes, *American Journal of Public Health*, February, 1956.

VERTEBRAL OSTEOPHYTOSIS

A CLINICAL SYNDROME

Edgar M. Bick, M.D., New York

• *Vertebral osteophytosis is a proliferation of bone that occurs within the intervertebral ligaments at their insertions into the apophyseal rings of the vertebral bodies and gives the effect of lipping in roentgenograms.*

It is sometimes asymptomatic. When painful symptoms do occur, they are likely to return with variable intensity at intervals during a period of two to four years. If they occur in the thoracic region, differential diagnosis is urgent because the pain may simulate that of coronary disease and other important conditions. Uncomplicated vertebral osteophytosis is self-limited, responds easily to rest and support, and only occasionally requires palliative measures.

The most frequently occurring lesion of the spine, certainly one of the oldest known, vertebral osteophytosis has paraded under a variety of misnomers and had almost universal misinterpretation ever since its discovery. It has been popularly grouped with the spinal arthritides, usually as osteoarthritis, or under its older terminology, hypertrophic arthritis. For several decades following the publication of a book by Knaggs [1] in 1926, it was often confused with ankylosing spondylitis. Shore encouraged the arthritic interpretation by describing the lesion as a special variety of spondylitis under the name polyspondylitis marginalis osteophytica.[2] In more recent decades it has been casually referred to as lipping of the spine. This, at least, evaded the question of its pathology. Schmorl and Junghanns,[3] and later Collins,[4] related vertebral osteophytes found at autopsy to degeneration and herniation of the intervertebral disks.

Pathology

The unique histopathology of vertebral osteophytosis has recently been described.[5] Pathologically it is an osteogenic proliferation occurring within the vertebral ligaments at their insertions into the apophyseal rings of the vertebral bodies.[6] The ossific masses vary in size from that of a lentil to a large double plaque crossing the intervertebral space. Pathogenically they are the characteristic reaction to strain found at the insertions of powerful ligaments into bone at many sites throughout the axial and appendicular skeleton. This phenomenon is well recognized along the iliac crests, at the femoral adductor tubercle, and at the insertion of the long plantar ligament into the calcaneus.

Osteophytes tend to appear wherever persistent strain is exerted on the insertion of connective tissue into bone. At their phylogenetic maximum such strains produce apophyses to the body of the bone, as for example the trochanters of the femur and the tubercles of the humerus. At the level of individual abnormal stresses, osteophytes appear. In the spinal column of man, the insertion of the long vertebral ligaments into the bodies of the vertebrae may come under persistent strain from a variety of causes, including postural imbalance such as found in obese individuals of the pendulous-abdomen-sway-backed type [7] in adults with scoliosis, or from the imbalances that follow compression fractures of vertebrae.[8] Compensatory strains of these ligaments may follow degenerative changes of either the intervertebral disks [9] or the intervertebral articulations (osteoarthrosis vertebralis).[10] Similar spinal imbalances and osteophyte formations occur following the deformity of vertebral bodies due to menopausal, senile, or other osteoporotic syndromes.

Vertebral osteophytosis may appear as a single lesion, as distinct lesions in several parts of the spine, or with widespread distribution involving all the segments of the vertebral column. The numerical difference in occurrence at the cervical, thoracic, or lumbar levels is statistically insignificant. In the cervical spine, more than elsewhere, it is frequently, though not necessarily, associated with disk degeneration. Osteophytes are found most often in the anterior longitudinal ligaments, secondly in the lateral ligaments, and least often in the posterior ligaments (see figure).

Painful Symptoms

Vertebral osteophytosis may cause painful symptoms at any stage of its development. Symptoms are apt to be recurrent with variable intensity. Pain may appear only in certain postural positions or may occur without known precipitating factors. Often enough an advanced degree of vertebral osteophytosis may be incidentally discovered in an elderly patient whose only symptoms have become a historically remembered occasional backache. In its most advanced stages it is apt to be quite without symptoms and suggests the salutary occurrence of spontaneous and healing fusion.

From the Orthopedic Service, Mount Sinai Hospital.

Read before the Section on Orthopedic Surgery at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 7, 1955.

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In general, smaller osteophytes are apt to be asymptomatic incidents, or at least difficult to relate to a presenting symptom. As the osteophyte grows it inevitably interferes with the normal mobility of the spinal column at the affected level. In the presence of degenerative changes in the intervertebral or intra-articular tissues associated with osteophytes of considerable size, it may become a speculative question as to which lesion is primary. The mechanical interference caused by a large primary osteophyte due to postural strain may well condition degenerative changes in other elements of the spinal column. Conversely, the strains put upon the longitudinal vertebral ligaments in the presence of primary vertebral degenerations may have stimulated the production of the osteophyte.

The cause of localized back pain in primary vertebral osteophytosis is difficult to determine. Lindblom in 1950, with his ingenious experiments in discography, demonstrated a high concentration of pain-sensory nerve endings in the vertebral ligaments.[10] When pain does occur in this syndrome, it may be localized to the affected area and marked by local tenderness to deep pressure. More often the ache is diffused about the affected spinal segment, expressing perhaps the pain of reflex protective muscle spasm or the strain of contiguous spinal ligaments and fascia. At times, even in primary osteophytosis, pain exhibits characteristic radiations due to indirect pressures on the nerve roots. Such radiations would be brachial in cervical involvement and sciatic or lateral femoral cutaneous in lumbar lesions.

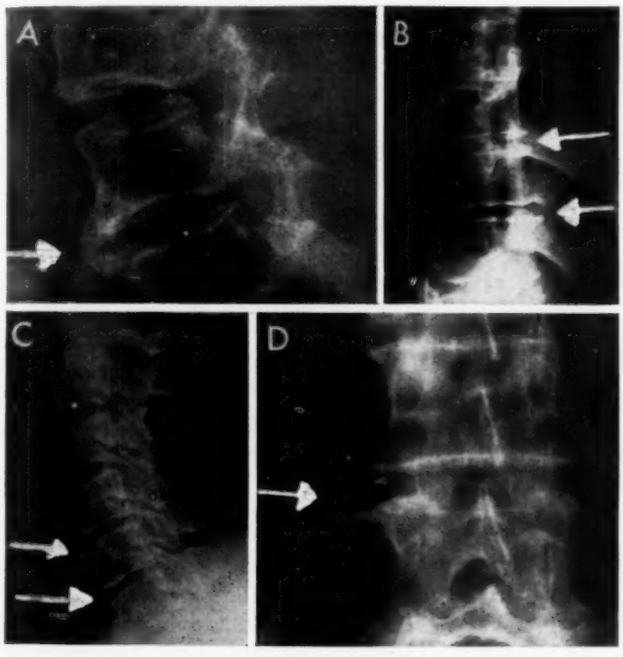

Fig. 1.—Roentgenograms showing, *A*, bridging solitary vertebral osteophyte, primary, lumbar, involving anterior longitudinal ligament; *B*, multiple vertebral osteophytes, primary, thoracic, involving lateral longitudinal ligament; *C*, multiple vertebral osteophytes, primary, cervical, involving anterior longitudinal ligaments; and, *D*, solitary aberrant vertebral osteophytes, primary, lumbar, involving paravertebral ligaments.

When radiating pains occur from osteophytosis in the thoracic spine a diagnostic problem of utmost urgency is presented, since, depending on the roots involved, such pains may simulate coronary disease, mediastinal disease, or, in the lower thoracic level, any of the visceral lesions of the upper abdomen. Ascribing such symptoms to vertebral osteophytosis of the thoracic spine must, of necessity, be a matter of diagnosis by exclusion, since experience has emphasized the high probability of asymptomatic lesions, especially in this segment of the vertebral column.

When vertebral osteophytosis is primary, that is, uncomplicated by associated articular or disk deterioration, or deformity of the vertebral body, symptoms are almost always self-limited and the patient is relieved by rest in a firm bed or by wearing a spinal support. At times, especially at the onset, palliative measures such as local heat, medication, or muscle-relaxing drugs may hasten relief. Within a period of two to four years symptoms are apt to recur. Ordinarily at the end of this time the osteophytes appear to have attained a mechanically satisfactory degree of expansion in which the local stresses and strains are stabilized. In fact the attainment of such stability might be considered the teleological objective of osteophytosis. With decrease in intensity of symptoms, the spinal support is gradually discarded. It has become a continuing experience that, when the symptoms of vertebral osteophytosis persist or worsen under a regimen of these simple measures, other lesions should be sought, even though they are not evident at the first instance.

Summary

Vertebral osteophytosis is a unique syndrome of the spinal column. It is often associated with traumatic or spontaneous degenerations or with inflammatory lesions of the spinal column, to which it may be considered a protective or corrective response. In itself, however, it is none of these. Particularly, it is not spinal arthritis, hypertrophic, or otherwise, nor is it inevitably a mark of disk disease. It is therapeutically misleading to continue to so describe it. When vertebral osteophytosis appears secondarily as a response to other lesions, it should be so stated in the diagnosis, since, from the point of view of treatment, the preceding lesion is far more apt to be the more urgent. Symptomatically, uncomplicated vertebral osteophytosis is a self-limited syndrome in which the patient responds easily to rest and spinal supports and only occasionally requires simple palliative measures.

Thrombosis and Carcinoma.—Obscure carcinoma should be considered in cases of recurrent migrating thrombophlebitis which cannot be attributed to any of the known associated causes as operations, pregnancy, blood dyscrasias, thromboangiitis obliterans, prolonged bed rest, etc. A thorough search should be made of the various organs, with use of all available diagnostic methods. Although in most of the reports of carcinoma so discovered the lesion was inoperable, in a few an operable neoplasm was found. It is possible that greater awareness on the part of the physician of the possible association of venous thrombosis and carcinoma may result in earlier diagnosis and increase the number of operable cases. . . . Anticoagulant therapy [does] not prevent progression of the venous thrombosis or involvement of new areas or pulmonary embolism in these cases. . . . A gastrointestinal carcinoma [may] bleed, sometimes profusely, when the patient is receiving anticoagulants. . . . Administration of an anticoagulant and examination of the stool for blood may often aid in the diagnosis of gastrointestinal carcinoma.—Samuel Perlow, M.D., and J. L. Daniels, M.D., Venous Thrombosis and Obscure Visceral Carcinoma, *A. M. A. Archives of Internal Medicine*, February, 1956.

HIATAL HERNIA AND RELATED DISORDERS OF THE ESOPHAGOGASTRIC JUNCTION

E. Clinton Texter Jr., M.D., Hubbard W. Smith, M.D., H. Ivan Sippy, M.D.
and
Clifford J. Barborka, M.D., Chicago

• *In hiatal hernia of the sliding type the esophagogastric junction is drawn upward through the stretched esophageal hiatus of the diaphragm; in the rolling type, the esophagogastric junction is normally situated but an adjacent portion of the cardiac part of the stomach is squeezed in beside it. The two types therefore cause different symptoms.*

Although the most frequent symptoms are dysphagia, heartburn, and pain, they vary widely and are sometimes absent. The treatment depends on the symptoms, for hiatal hernias are rarely responsible for severe illness or complications.

In the first case cited, reflux of gastric contents had caused burning sensations that were explained by the finding of esophagitis by direct esophagoscopic examination. The hernia was of the sliding type, and the symptoms subsided during five months of conservative treatment with a bland diet and antacids.

The second case was complicated by the presence of a duodenal ulcer. Measurements of motility and the use of drugs to abolish hypermotility showed that both chemical and mechanical factors were involved in the causation of symptoms, and the heartburn was relieved by the patient sitting up, drinking water, or taking an antacid.

Hiatal hernia is a condition that is becoming more prevalent with the increasing longevity of the population. It is the second most frequent diagnosis in patients undergoing x-ray study of the upper gastrointestinal tract, the incidence being nine per cent.[1] In elderly patients the incidence may be as high as 33%. Two basic types of hiatal hernia are described. Type 1, also termed the sliding or short esophagus type, is the result of the stomach sliding directly through both the membranous and muscular openings of the diaphragm so that the esophagogastric junction is above the diaphragm. Type 2, also termed the rolling or paraesophageal hiatal hernia, is the result of herniation of the gastric cardia through the hiatus, so that the stomach is adjacent to the normally situated esophagogastric junction (fig. 1). The primary difference between the two types of hernia lies in the angle of entry of the esophagus into the stomach. In the sliding type the cardia is patulous, while in the rolling type the angle of entry is acute. Reflux esophagitis is more common in the sliding than in the rolling type of hiatal hernia.

Hiatal hernias were formerly classified into the short esophagus and the paraesophageal types. The short esophagus hiatal hernia was thought to result from congenital shortening of the esophagus. This concept ignored the intrinsic contractile power of the esophagus when it is freed from its normal attachments. Actually, the majority of patients having the so-called short esophagus type of hiatal hernia have shortening of the normal esophagus. True congenital shortening of the esophagus is rare. Belsey [2] indicates that the diagnosis of congenital short esophagus should not be made except at operation, when muscular contraction can be overcome and the length of the esophagus relative to adjacent structures can be actually measured.

The occurrence of hiatal hernia in infants suggests that the disease is fundamentally of congenital origin as the result of developmental abnormalities of the diaphragm. These abnormalities include congenital deficiency of the right crus of the diaphragm and the posterior margin of the hiatus [3] and defect in the phrenoesophageal ligament.[4] Increased intra-abdominal pressure during pregnancy, the accumulation of abdominal fat, and decrease in the tone of the diaphragm contribute to the development of hiatal hernia. Hiatal hernia is frequently found in association with other unrelated diseases. The incidence of concomitant radiological evidence of gastrointestinal disease in patients with hiatal hernia has been reported as 25%.[1] The most important gastrointestinal conditions are peptic ulcer,[5] cholelithiasis,[6] and gastrointestinal diverticulosis.[7]

Symptomatology

The symptoms of patients with hiatal hernia are variable. Patients may be entirely asymptomatic, the diagnosis being made incidentally at the time of roentgen study. Patients with symptoms may be divided into two groups: those whose symptoms are not specifically related to the esophagus, and those who have symptoms specifically related to the esophagus. The percentage of patients having symptomatic hiatal hernia varies con-

From the Gastroenterology Laboratory, Northwestern University Medical School, the Veterans Administration Research Hospital, Passavant Memorial Hospital, and Chicago Wesley Memorial Hospital.

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This paper was reviewed by the Veterans Administration and is published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

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siderably in reported studies.[8] In our experience, careful questioning reveals that the majority of patients have symptoms referable to the hiatal hernia. The propensity of esophageal hiatal hernias to produce pain resembling anginal pain is well known. The symptoms of hiatal hernia may simulate those of other diseases. When other diseases are present it is difficult to determine whether symptoms are attributable to the hiatal hernia.

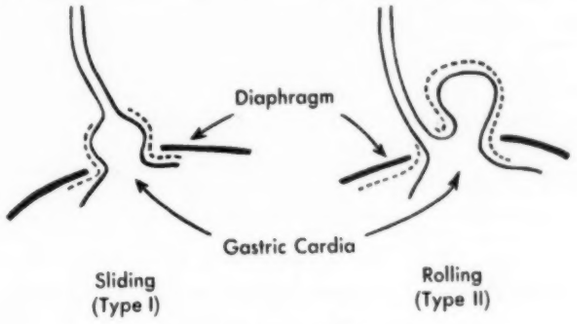

Fig. 1.—Types of hiatal hernia.

The most frequent symptoms associated with hiatal hernia are dysphagia, heartburn, and pain. Regurgitation and belching may also be reported. The esophageal symptoms may be altered if inflammatory changes occur in the distal esophagus. Abnormalities of the closing mechanism at the esophagogastric junction may result in regurgitant esophagitis or localized ulceration of the esophagus or of the herniated stomach. The patient may develop complications such as hemorrhage, perforation, or obstruction. There is an additional group of patients with regurgitant esophagitis in whom no hiatal hernia can be demonstrated roentgenographically. Reflux of gastric contents into the esophagus can be demonstrated.[9] Regurgitation through the patulous cardiac orifice has been suggested as a cause of the esophagitis and symptoms.[2]

In patients with asymptomatic hiatal hernia, diagnosis is made at the time of x-ray study of the stomach. The hernia may not be demonstrated with the patient in the upright position, but when the patient is placed in the Trendelenburg position, barium can be seen to enter the esophagus from below. Increase in intra-abdominal pressure enhances the value of the Trendelenburg position in the demonstration of the hernia. Esophagoscopic examination is of most value in demonstrating inflammatory changes of the distal esophagus. With the more frequent use of esophagoscopy, mucosal changes are found to be more common than thought heretofore. A good correlation exists between the endoscopic appearance of the mucosa and the clinical condition of the patient. In patients with uncomplicated hiatal hernia the esophageal mucosa is gleaming and of normal color. With the development of esophagitis, the mucosa of the lower esophagus becomes hyperemic and edematous.

CASE 1.—A 48-year-old man complained of a burning sensation in the lower chest after the ingestion of tea, coffee, or spices. A smooth constriction in the lower third of the esophagus compatible with esophagitis was shown radiologically. Esophagoscopic examination revealed esophagitis. Repeat examination after five months of treatment with a bland diet and antacids demonstrated improvement in the esophagitis and a sliding type of hiatal hernia.

Physiological Basis for Symptoms

Dysphagia.—Understanding the mechanism of dysphagia in patients with hiatal hernia has been aided by the study of intraluminal pressures of the esophagus with multiple open-end catheters. The deglutition pressures have been correlated with esophageal transport as revealed by x-rays after a barium meal. Three no. 10 F. catheters with their ends 5 cm. apart are employed to measure the pressure at the esophagogastric junction, the distal esophagus, and the lower midesophagus simultaneously. The end of the distal catheter was placed just above the diaphragm. In some of the patients with hiatal hernia, it could be seen in the herniated thoracic stomach. A strain gauge is connected to each of these tubes, and their output is applied to a carrier amplifier that records continuously. With this technique the basal pressures of the esophagus and the pressures produced by swallowing have been measured. The peristaltic wave normally traverses the esophagus in about 8 seconds and develops pressures up to 100 mm. Hg.[10] The most distal portion of the esophagus, the vestibule, is characterized by lower pressures and delayed or absent propagation of the peristaltic wave.[10b]

The generalized decrease or absence of deglutition pressures throughout the esophagus has been observed in patients having dysphagia as the result of cardiospasm (fig. 2). Similar observations on patients with hiatal hernia demonstrated decreased deglutition pressures at the esophagogastric junction and the herniated stomach, with normal pressures in the more proximal esophagus. The prolongation of the duration of the peristaltic waves at the junctional area in the hiatal hernia group was com-

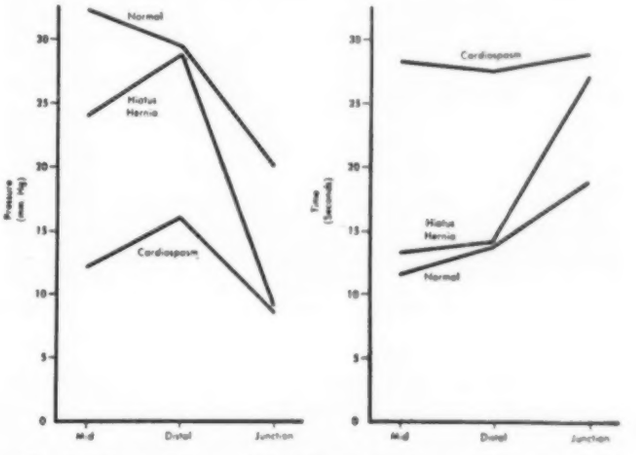

Fig. 2.—Mean pressure and duration of swallow complexes at the mid, distal, and junctional areas of esophagus in normal subjects and patients with hiatal hernia and cardiospasm.

parable to that seen in cardiospasm. These findings suggest that the lower deglutition pressures at the esophagogastric junction and the herniated stomach may account

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for the dysphagia of patients with hiatal hernia even in the absence of inflammatory changes of the distal esophagus.

Heartburn and Pain.—The physiological basis of heartburn is not clearly understood. It is commonly held that heartburn is the result of regurgitation of acid gastric contents into the distal esophagus.[9] However, heartburn is common in pregnancy, when the acid levels are low and achlorhydria is frequent.[11] Heartburn may also occur in patients with achlorhydria as the result of gastric surgery. Heartburn is most likely to follow the ingestion of acid, spicy, carbonated, or very hot or cold substances. The symptoms of heartburn can be reproduced by cholinergic drugs, by distention of the esophagus with a balloon, or by local instillation of ice water. Instillations

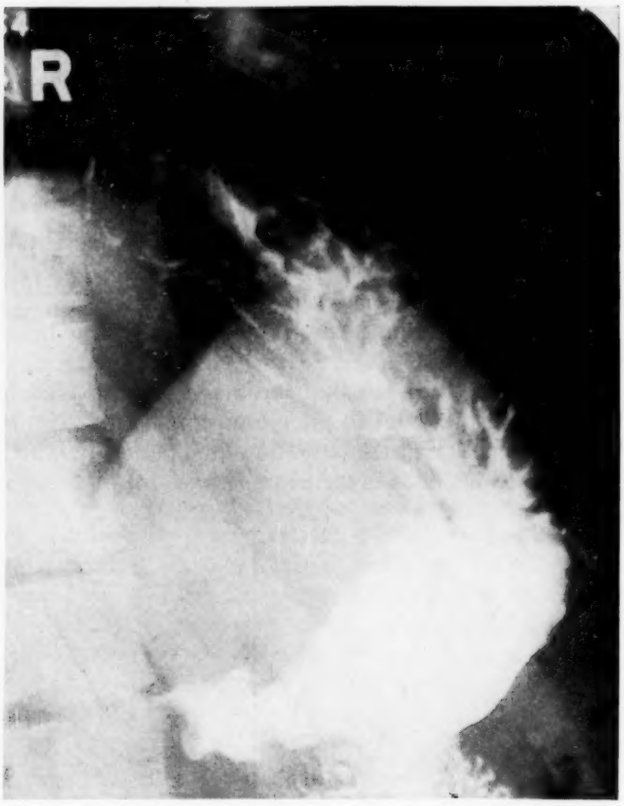

Fig. 3.—X-ray showing large rolling hiatal hernia and deformed duodenal bulb (case 2).

of inert solutions at a rapid rate may also cause symptoms. Jones [12] has suggested that the symptoms of esophageal disease are fundamentally due to motor disturbances mediated by the autonomic nervous system. Measurement of the intraluminal pressures of the esophagus is also being used to study the mechanism for esophageal pain and heartburn. The simultaneous use of a barium-hydrochloric acid suspension facilitates study of the esophageal motility as well as increasing the acid level in the stomach.[13] An example of one of these studies follows.

CASE 2.—A 35-year-old man had had intractable ulcer pain for several months. He also complained of heartburn. X-ray studies demonstrated a hiatal hernia and duodenal ulcer (fig. 3). Intraluminal pressures in the stomach and duodenum were measured, after which 200 cc. of hydrochloric acid-barium was instilled into the stomach. The patient developed heartburn almost immediately and a severe ulcer pain within a few minutes. Hypermotility of the antrum was evident fluoroscopically and was also shown by the pressure changes. After administration of 20 mg. of propantheline (Pro-Banthine) bromide intravenously, both the ulcer pain and the heartburn subsided within three minutes. The hypermotility was abolished by propantheline bromide. Heartburn returned again 20 minutes later as the tubes were withdrawn from the stomach into the esophagus. Secondary contractions resembling those seen in cardiospasm were observed. The heartburn was relieved by the patient's sitting up, drinking water, or taking an antacid.

Treatment

The treatment of hiatal hernia and related conditions depends upon the symptoms that are present. Fortunately, only a small proportion of hiatal hernias are responsible for severe illness, and complications are rare. Most patients can be handled satisfactorily in a conservative manner. The treatment is similar to that for peptic ulcer, consisting of the use of a bland diet, antacids, and antispasmodics. Elevation of the head of the bed and the patient's maintaining the erect position for at least one hour after eating are of value in preventing regurgitation into the esophagus. Reduction of excess weight, relief of constipation, and the avoidance of constricting abdominal garments are also useful, since they tend to lower intra-abdominal pressure. If the hiatal hernia becomes complicated by the development of peptic esophagitis, more vigorous treatment is necessary. The dietary and antipeptic program should be followed rigorously. Mechanically and chemically irritating foods, hot and cold drinks, and highly seasoned foods should be avoided. Bismuth subcarbonate, which coats the inflamed mucosa and is also mildly antacid, is useful. The dose is 2 gm. after meals, between meals, and upon retiring. Similar treatment is prescribed for a local esophageal ulcer.

Certain complications may require special treatment. A frequent complication is that of stricture. In most instances this can be handled satisfactorily by dilatation of the esophagus. Bleeding is a serious complication and, if massive or severe, carries a serious prognosis. Palmer [6] recommends cauterization of the bleeding point with silver nitrate or packing the segment with oxidized cellulose (Oxycel). Balloon tamponade may also be helpful. Spontaneous perforation of the esophagus constitutes a real surgical emergency. The usual procedure consists of mediastinotomy followed by closure of the defect and drainage, with concurrent administration of antibiotics. The major indication for surgery is failure of medical management. Repair of the hiatal hernia may be carried out with one of several techniques. If severe esophagitis accompanies a hiatal hernia, either gastrectomy or vagotomy with gastroenterostomy may be required also. Resection of the stenosed segment with performance of an esophagogastrostomy may be necessary if obstruction develops in the distal esophagus.

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The evaluation of the results of treatment is difficult. For most patients with uncomplicated hiatal hernia, satisfactory control can be achieved with medical means. Those patients who require surgery usually have more serious difficulty with their disease. The postoperative morbidity is a serious problem, and recurrences develop in some patients. Even in the absence of a demonstrable recurrence, some patients may have persistence of symptoms.

Summary

Hiatal hernia is a common disorder that increases in frequency with increasing longevity of our population. The condition is fundamentally of congenital origin, but its incidence is increased by conditions that raise intra-abdominal pressure. The symptomatology is variable; the disease may be asymptomatic, may mimic other conditions, or may present symptoms referable to the esophagus. The most common symptoms arising from the esophagus are dysphagia, pain, and heartburn. When the condition is suspected clinically, the diagnosis is establishd by the use of roentgen study and by esophagoscopy. The symptoms appear to result from alterations of motor function of the esophagus and herniated stomach as well as from regurgitation. Treatment is primarily medical, but surgery is necessary for patients whose condition is intractable to medical treatment or who develop complications secondary to inflammation and erosion of the esophagus.

303 E. Chicago Ave. (11) (Dr. Texter).

CONSERVATIVE TREATMENT OF CARCINOMA OF THE PROSTATE

Thomas L. Pool, M.D.
and
Gershom J. Thompson, M.D., Rochester, Minn.

• *The case records of 1,560 patients who had carcinoma of the prostate were reviewed. Transurethral prostatic resection was performed in each case. During the 20 years represented by this series the percentage of patients who lived five years or more after operation increased steadily, and in the period from 1942 to 1946 it was 39.2%. The improvement is only in part attributable to the advent of orchiectomy and hormone therapy, for it is seen also in other types of cancer.*

The average amount of tissue removed was less than 20 gm. The removal of less than 30 gm. sufficed to relieve the urinary obstruction in the large majority of patients, and only 173 had to return for reoperation in later years.

The grades of malignancy assigned to the lesions on pathological examination were strongly correlated with survival time. Five patients in whom metastasis had occurred were strikingly benefited by orchiectomy and/or diethylstilbestrol by mouth. A spirit of optimism should be maintained in the treatment of any patient with carcinoma of the prostate.

In the past 30 years there has been a tremendous change in the outlook of a patient suffering from carcinoma of the prostate gland. Many such patients may live for a long time, may live useful lives, and may be free from suffering and pain. No longer is it necessary to dismiss a patient with carcinoma of the prostate and expect to have him return soon asking for opiates to relieve his suffering. Our wish is that all such patients could expect a cure. It is our opinion that there has been too much pessimism in dealing with patients who have carcinoma of the prostate gland. This has been engendered by inadequately informed physicians and magnified by relatives when such a condition is encountered. Such patients should be treated with optimism. Later on, we shall present statistical data that will justify an optimistic outlook for patients with carcinoma of the prostate.

Radical Excision

Physicians agree that radical excision of prostatic carcinoma, or any carcinoma for that matter, is a desirable end. This means that early diagnosis is something devoutly to be wished. We are defeated in this since so many patients with prostatic carcinoma are unaware that anything is wrong with them. Yearly physical examination, including rectal palpation of the prostate gland, is being stressed more and more. Even with such a survey, in many patients prostatic carcinoma will develop in the interim, and it will, if high grade, have proceeded, by the time set for the next examination, to grow to an inoperable state as far as radical excision is concerned.

Years ago, reports revealed that only 4% of patients with carcinoma of the prostate gland were suitable candidates for radical perineal prostatectomy. More recent statistics have given higher figures; some of these figures are as high as 10%. We believe that 90 to 95% of patients with carcinoma of the prostate cannot be considered as candidates for either a radical perineal or a radical retropubic type of procedure.

We cannot agree with the proposition that more patients with prostatic carcinoma can be successfully treated by a radical operation since the advent of hormonal therapy than before the use of such therapy. Hormonal therapy might make an operation technically possible. However, knowing the nature of the disease, we seriously question whether malignant cells that have spread through the lymphatics and to other viscera will

From the Section of Urology, Mayo Clinic and Mayo Foundation. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

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recede to the prostate or be totally destroyed by such treatment. It is our feeling that the present enthusiasm for extensive excision after hormonal therapy will subside in the years to come. By then, perhaps, our hope for the true cause of cancer may be established and therapy given through the blood stream will be effective. In carcinoma of the thyroid gland, much progress has been made. Perhaps someone will find some method of treating carcinoma of the prostate gland in a similar manner.

In the past five years, 56 patients with carcinoma of the prostate gland have been subjected to radical prostatectomy at the Mayo Clinic. These patients were among those seen by all members of our section, the personnel of which consists of seven urologists. Definite criteria have been imposed by all of us before considering such a procedure. In all of these patients a small nodule confined to the gland itself has been the lesion treated. In no case has hormonal therapy been used either preoperatively or postoperatively. Of course, it is too soon to report the results for this small series. Some interesting statistics should be found when such a review is made.

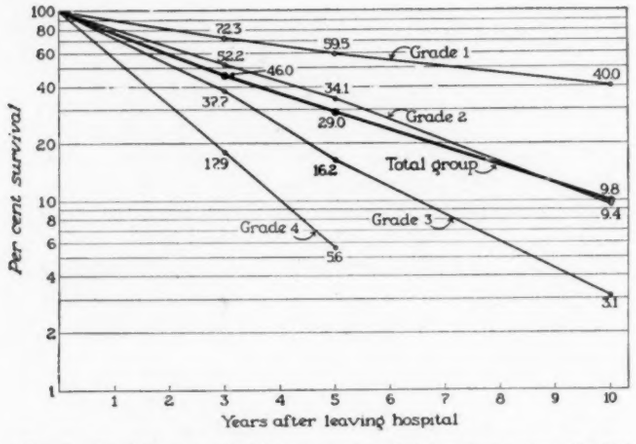

Fig. 1.—Survival rate according to grade of lesion in a series of 1,534 cases of prostatic carcinoma.

One point of interest should be mentioned; namely, that before a radical prostatectomy was performed the results of frozen-tissue biopsy had been reported as positive by the pathologist. If this step is omitted, serious mistakes may be made in the diagnosis of the exact lesion present. Two common offenders in this regard are small prostatic calculi and granulomatous prostatitis.

Incidence and Diagnosis

The incidence of prostatic carcinoma varies with each authority. Most agree that carcinoma of the prostate gland is more common in men than is any other malignant lesion. The simple statement first made years ago is probably as near the truth as we can come. Twenty per cent of men in the age when prostatic disease is most prevalent will give a story of obstruction requiring some type of surgical procedure, and 20% of these will have a carcinoma of the gland.

In the examination of a patient suspected of having a carcinoma of the prostate gland, routine studies as well as x-ray examination of the region of the kidney, ureter, and bladder should be made. If these are omitted, frequent errors in diagnosis may arise, since it is not uncommon to pick up unsuspected sites of metastasis. When carcinoma of the prostate spreads beyond the gland, it rapidly goes to many parts of the body, including bone, regional and distal lymph nodes, and the lungs and liver. In a series of 54 patients with extensive metastasis, the sites of involvement were as follows: lymph nodes, 66 (with 36 pelvic, 20 aortic, and 6 mediastinal); lung, 15; pelvic peritoneum, 10; bones of pelvis,7; lumbar segment of spinal column, 5; cervical segment of spinal column and ribs, one each; kidney, 5; liver and spinal cord, 3 each; mesentery and adrenal gland, 2 each; omentum, diaphragm, small intestine, and cecum, one each; direct extension to bladder, 7; seminal vesicle, 5; ureter, 6; and rectum, 2.

TABLE 1.—*Five-Year Survival According to Age Groups in Patients with Malignant Lesions of the Prostate Treated by Transurethral Resection of the Prostate, 1926 to 1946 Inclusive*

Age, Yr.	Patients		Lived 5 Yr. or More After Operation	
	Total	Traced	No.	% *
<60	169	167	52	31.1
60-69	635	619	201	32.5
70-79	609	602	170	28.2
80+	147	146	22	15.1
Total	1,560	1,534	445	29.0

* Based on traced patients. Inquiry as of Jan. 1, 1952.

These questions naturally arise: How can we know in any specific case whether metastasis has occurred? If the process seems confined to the gland, what studies can be done to prove the absence of disease elsewhere? We and in one-third of the patients with definite evidence of bony metastasis the level of acid phosphatase is still have found that the levels of phosphatase in the blood are not too reliable as diagnostic aids. The level of acid phosphatase is practically always normal when one fails to demonstrate metastasis to bone by x-ray examination, normal. We feel that the principal use of acid-phosphatase determinations is in judging progress when hormonal therapy is being used. Such determinations are of little or no value over and above x-ray examination in the detection of early metastasis.

TABLE 2.—*Five-Year Survival According to Periods in Patients with Malignant Lesions of the Prostate Treated by Transurethral Resection of the Prostate, 1926 to 1946 Inclusive*

Period	Patients		Lived 5 Yr. or More After Operation	
	Total	Traced	No.	% *
1926-1936	349	349	48	13.8
1937-1941	562	558	151	27.1
1942-1946	649	627	246	39.2
Total	1,560	1,534	445	29.0

* Based on traced patients. Inquiry as of Jan. 1, 1952.

Survival in a Series of Cases

In a recent study at the Mayo Clinic, the case records of 1,560 patients who had carcinoma of the prostate gland were reviewed. These patients were seen in the years

1926 to 1946 inclusive. Transurethral prostatic resection was employed in each case. Table 1 reveals that approximately 80% of these men were in the age group 60-79 years. A little more than 10% were less than 60 years of age, and a little less than 10% were 80 years of age

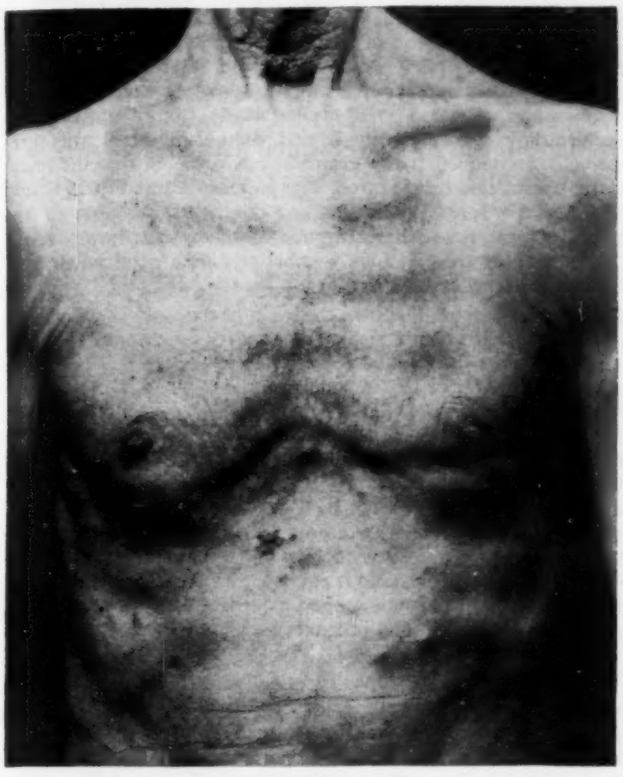

Fig. 2.—Numerous subcutaneous nodules. Biopsy disclosed grade 2 adenocarcinoma of prostatic origin. Complete regression of subcutaneous nodules was evident 12 days after orchiectomy.

or older. Also shown in this table is the fact that the five-year survival rate for younger men with prostatic carcinoma is as good as, or better than, the rate for those in the older age groups.

TABLE 3.—*Distribution of Patients According to Amount of Tissue Removed*

Tissue Removed, Gm.	Patients	
	No.	%
0- 9	417	27.4
10-19	562	37.0
20-29	287	18.9
30-39	121	8.0
40-49	60	3.9
50-59	37	2.4
60-69	23	1.5
70-79	5	0.3
80-89	3	0.2
90-99	4	0.3
100+	1	0.1
Total	1,520*	100.0
Largest	141 gm.	
Mean	19.3 gm.	

* In 40 cases there is no record of amount of tissue removed.

Table 2 shows the survival figures for three different periods. The first period represents a time that was well in advance of the advent of diethylstilbestrol (Stilbestrol) therapy or orchiectomy, the second period covers the five years immediately preceding hormonal therapy, and the third period represents the five years immediately after the advent of such treatment. One of the interesting figures is the change in five-year survival rate from 13.8% for the first period to 27.1% for the period that immediately preceded the advent of hormonal therapy. We feel that this reveals evidence of a decreasing lethal

TABLE 4.—*Five-Year Survival According to Grade of Lesion in Patients with Malignant Lesions of the Prostate Treated by Transurethral Resection of the Prostate, 1926 to 1946 Inclusive*

Grade	Patients		Lived 5 Yr. or More After Operation	
	Total	Traced	No.	% *
1	293	284	169	59.5
2	486	478	163	34.1
3	463	457	74	16.2
4	252	250	14	5.6

* Based on traced patients. In 66 cases, grade of malignancy is unknown. Inquiry as of Jan. 1, 1952.

effect of prostatic carcinoma. Men were surviving longer with such a carcinoma even without hormonal therapy. Others have found that carcinoma of the breast, carcinoma of the stomach, and carcinoma of the colon also exhibit this same trend. This would lead us to believe that survival figures in patients seen in the past decade are superior in all forms of carcinoma to those in patients treated two, three, or four decades ago. Of course, many patients of our series in the period 1942 to 1946 received diethylstilbestrol, and 80 of them had orchiectomy some years after transurethral resection, which might or might not have added to their longevity.

Table 3 shows the distribution of patients according to the amount of tissue removed by transurethral resection. The removal of less than 30 gm. was sufficient in the large majority of patients to relieve the urinary obstruction. One cannot claim that a radical type of operation was necessary to remove a sufficient amount of tissue. Of the 1,560 patients tabulated, only 173 found it necessary to return for a subsequent operation in later years. For most of them, the single prostatic resection was enough.

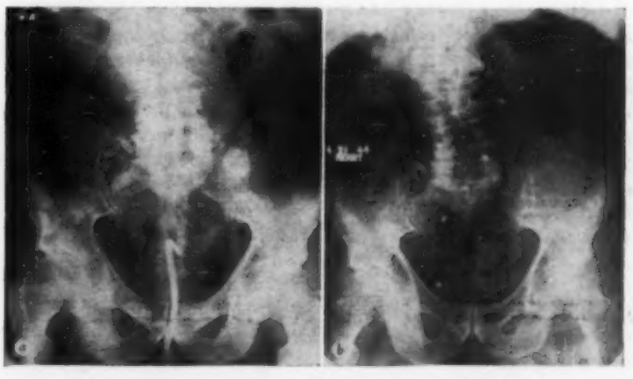

Fig. 3.—*A*, large islands of osteoplastic metastasis. *B*, two years later, bones entirely clear of metastatic lesions.

Table 4 reveals that the grade of the lesion has an important bearing on survival of the patient. The grade 4 tumor is lethal, since only 5.6% of patients with this lesion survived 5 years or more and none survived 10

years. Figure 1 represents curves projecting the longevity out to 10 years. It is to be noted that 40% of patients with grade 1 lesions lived 10 years or more. These were not so-called occult cancers. Two-thirds of them were substantial in size, not just small nodules. The following cases illustrate the value of hormonal therapy and the effect of orchiectomy.

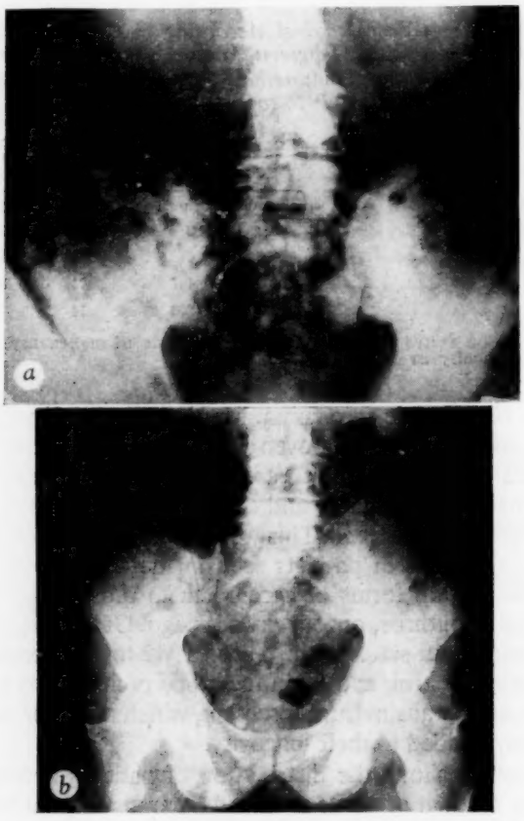

Fig. 4.—*A*, extensive involvement of the vertebral column and the innominate bones. Note the numerous irregular patches in the third and fourth lumbar vertebrae. *B*, third and fourth lumbar vertebrae and upper part of innominate bones are clear.

Report of Cases

CASE 1.—Figure 2 shows a man 64 years of age who, on his second visit to the Mayo Clinic, presented the subcutaneous nodules shown in the figure. Almost a year earlier, transurethral prostatic resection had been carried out because of symptoms of obstruction. Grossly, the tissue removed appeared to contain a malignant lesion, but none was found on pathological examination at that time. However, when the patient returned, he had a subcutaneous nodule that, when removed and examined, appeared to consist of tissue exactly like that of prostatic carcinoma. Reexamination of the prostatic tissue removed the year before revealed positive evidence of malignancy. Bilateral orchiectomy was performed. Twelve days later, the skin was smooth. Diethylstilbestrol was prescribed. When the patient was seen more than five years after the first operation, he had gynecomastia but no clinical evidence of carcinoma. X-ray examination of the spinal column and pelvis gave negative results, and phosphatase levels have always been normal.

CASE 2.—Figure 3 shows the roentgenograms of a man 82 years of age who underwent transurethral resection of the prostate and bilateral orchiectomy on Feb. 25, 1942, for a grade 3 adenocarcinoma. In spite of extensive metastasis (fig. 3*A*), acid phosphatase measured only 4.4 and alkaline phosphatase 17.2 King and Armstrong units per 100 cc. of serum. Two years later, x-ray examination revealed no evidence of metastasis (fig. 3*B*). At that time, the acid phosphatase measured 1.5 units and the alkaline phosphatase 3.9 units. The patient died in 1948, which was six years and five months after the operation. He was then 89 years of age. At the time of death he had no urinary symptoms. Of interest is the fact that the carcinoma was not the cause of death.

CASE 3.—Figure 4 shows the roentgenograms of a man 63 years of age who complained of urinary obstruction of three months' duration. On Sept. 25, 1937, transurethral prostatic resection was done and a total of 13 gm. of tissue was removed; the pathologist reported grade 3 adenocarcinoma. X-ray examination of the region of the kidney, ureter, and bladder gave negative results. No hormonal or other therapy was carried out. The patient returned in March, 1942. At that time, x-ray examination revealed marked metastasis (fig. 4*A*). Bilateral orchiectomy was performed, and diethylstilbestrol was prescribed. Subsequent x-ray examinations revealed that the metastatic lesions had disappeared. The patient returned in 1947 and again in 1948 for reexamination. X-ray examination of the spinal column revealed recurrence of metastasis; however, the distribution of these lesions was entirely different from that of the lesions seen earlier (fig. 4*B*).

CASE 4.—Figure 5 shows the roentgenograms of a man 54 years of age in whom metastasis to a rib developed within a nine-month period. His local physician examined him and made a roentgenogram of the thorax, which did not disclose any abnormality (fig. 5 *top*). He became seriously ill soon after this examination and, when seen at the Mayo Clinic nine months later, he had osteolytic metastatic lesions in the fourth rib on the left posteriorly (fig. 5 *bottom*). He had uremia and carcinoma of the prostate as palpated per rectum. Bilateral orchiectomy was performed. In less than two months the concentration of blood urea had returned to normal. In six months the rib had recalcified and the metastatic lesion was resolved. This case shows clearly how suddenly an inoperable lesion may appear within a period of months. The patient has received remarkable palliation from castration.

CASE 5.—Figure 6 shows the roentgenogram of a man who came to the Mayo Clinic because of multiple nodules in both pulmonary fields. He was found to have a carcinoma of the prostate as palpated per rectum. He was given diethylstilbestrol by mouth, and in eight months the x-ray appearance of the thorax was normal.

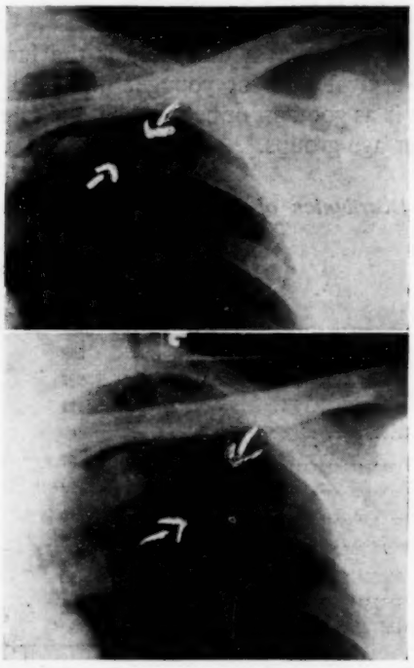

Fig. 5.—*Top*, normal rib seen on the left just below clavicle (posterior part of fourth rib). *Bottom*, complete osteolysis of this rib.

Various Therapeutic Procedures

Transurethral resection alone or in combination with orchiectomy or hormonal therapy is a conservative means of handling patients with carcinoma of the pros-

tate gland. Many other methods have been used. One of these, irradiation therapy, has long been considered a means of combating such malignant lesions. X-ray therapy alone has not been very successful in our hands in the treatment of the primary tumor. Such treatment is of value in helping alleviate the pain of metastatic lesions. Radium, radon, and, now, material such as radiogold injected into the gland have all been used in patients with prostatic carcinoma. Radium and radon have now almost been abandoned. Radiogold has been used with success, but the final outcome of such therapy has yet to be evaluated, and such a survey will be interesting.

Administration of cortisone for prostatic carcinoma has been advocated by many, and scattered reports would lead us to believe that it may be of value, particularly if there is widespread metastasis. Also, in combination with some estrogenic substance cortisone may prove highly beneficial. However, no survey has been complete enough to warrant high hopes of such medication. Cortisone in itself is a substance to be given only when the danger involved is a recognized one, since the use of this material causes atrophy of the cortex of the adrenal gland.

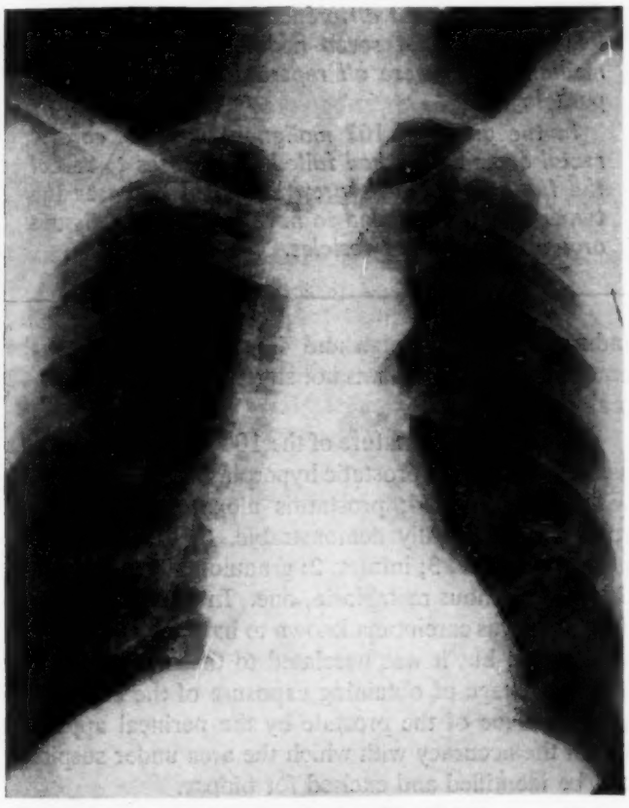

Fig. 6.—Numerous nodules in both pulmonary fields, but especially on the right. In eight months there was complete resolution of the nodules and pulmonary fields were normal.

Bilateral adrenalectomy has been advised for patients with prostatic carcinoma, and reports of series of cases have been published by various authors. The results are still confusing, and the subject remains a controversial one. Removal of the pituitary gland or irradiation of it to cause atrophy has been tried on many occasions. Results of such trials have not been spectacular.

One final word should be added concerning the resurgence that a malignant disease such as carcinoma of the prostate gland may exhibit. We have all seen patients who are suffering from such a lesion seemingly respond well for a varied period. Suddenly a change for the worse is noted, and the former therapy is of no avail. Then a change of program must be instituted. At times this is of value, but usually such is not the case and no program or combination of forms of therapy makes much change for the better. Because of this resurgence, many authorities feel that hormonal therapy or castration should be withheld until needed as a final resort. This is a moot point, and no final answer is now available. Some authors seem to feel that the early use of such therapy should be given prime consideration.

Conclusions

Carcinoma of the prostate gland can seldom be detected early enough to permit radical surgical treatment. For a great majority of patients, conservative treatment alone is indicated. In spite of this, a spirit of optimism should be maintained in the treatment of any patient with such a carcinoma, and such optimism is well justified. Relief of obstructive urinary symptoms by transurethral prostatic resection and the resulting prevention of the effects of infection and back pressure on the upper part of the urinary tract must be the main objective in most patients suffering from carcinoma of the prostate. Whether hormonal therapy, with castration or alone, is to be used early must be decided in each individual case. Also, when widespread metastatic lesions appear, the use of cortisone and irradiation therapy must be considered. It is our hope that some form of material will become available soon that can be used intravenously to combat the ravages of carcinoma of the prostate. The use of radical surgical measures such as bilateral adrenalectomy hardly seems justified at the present time. However, when nothing else seems to be of benefit, such measures should be considered.

It should be reemphasized that one should not be discouraged when treating patients with carcinoma of the prostate gland. The patient or his family should be informed of the condition, and a definite program for care should be instituted. The patient must be urged to return for reexamination at regular intervals for study of his situation and, if necessary, for alteration of the form of therapy. If such measures are carried out, the patient will continue to have confidence in his physician and will not fall into the hands of the so-called cancer quack.

Postmortem Skin for Grafts.—Although homografts provide only a temporary coverage for the wound, they may be lifesaving in extensively burned patients. Their application allows a period of time during which the general condition of the patient may be improved, and they prevent invasive infection. The use of skin from a cadaver is much more practical than homografts from living donors. Clinical experience with postmortem homografts during the past two years has demonstrated the success of these grafts in extensively burned patients. . . . Grafts were removed from donor bodies from three to seven hours after death. They survived from 2 weeks to 47 days. The use of postmortem homografts provides an easy, practical method of achieving temporary wound closure in extensively burned patients.—Lieut. Col. C. P. Artz, Capt. J. M. Becker, Capt. Yoshio Sako, and Capt. Alvin W. Bronwell, (MC), U. S. Army, Postmortem Skin Homografts in the Treatment of Extensive Burns, *A. M. A. Archives of Surgery*, November, 1955.

SIGNIFICANCE OF THE PALPABLE PROSTATIC NODULE

Hugh J. Jewett, M.D., Baltimore

• *Localized, abnormally indurated nodules found in the prostate gland were studied histologically in 211 cases; 108 were classified as benign and 103 as malignant. These results were compared with those of the preoperative digital rectal examinations to see whether the character of the nodule could be predicted from its location and consistency.*

Benign and malignant nodules differed little as judged by palpation. They were almost equally elevated or not elevated, smooth or irregular. Stony induration was present in 75 benign nodules. There was no great difference as to location within lobes, except that seven nodules palpated in the median furrow were all reported as benign by the pathologist.

In the group of 103 malignant nodules, careful rectal examination had failed in 74 cases to reveal the full extent of the growth, and in 26 cases the tumor cells were found to have invaded the tissues around the seminal vesicles.

The nodule as herein defined is a grossly circumscribed area of palpable induration confined to a portion of one prostatic lobe. Contrary to prevailing opinion, almost 50% of such nodules (fig. 1) are found to be malignant on microscopic examination of the tissue. In general, the malignant nodule has no palpable characteristics that can be relied upon to distinguish it from the benign.

From 1905 to 1955, 211 localized nodules of markedly abnormal induration were exposed perineally and subjected to accurate histological examination at the Johns Hopkins Hospital. In 72 cases operation was done between 1905 and 1945 and in 139 between 1945 and 1955. The fact that the number of cases seen within the last 10 years was nearly double the number during the preceding 40 years is evidence that the family physician is becoming increasingly aware of prostatic cancer and the benefit afforded by radical perineal prostatectomy in early cases.[1]

Of the total series of 211 palpable nodules, 108 were benign and 103 malignant. The great majority were found in men between 50 and 70 years of age. In the benign group the youngest patient was 40 years of age and in the malignant group, 43. In these two groups the recorded gross characteristics as detected by digital rectal examination were strikingly similar. Benign and malignant nodules occupied the same areas within the prostate gland, with the exception of the median furrow or groove: 30 benign and 41 malignant nodules were found in the apex of a lobe, 25 benign and 32 malignant in the center of a lobe, 39 benign and 30 malignant in the base of a lobe, and 7 benign and no malignant in the median furrow; the location of 7 benign nodules was not stated. The nodules were almost equally elevated or not elevated, smooth or irregular. Thirty-seven benign and 36 malignant nodules were elevated and 7 benign and 4 malignant not elevated; the prominence of 64 benign and 63 malignant nodules was not stated. Twenty-nine benign and 22 malignant nodules were smooth and 7 benign and 10 malignant irregular; the condition of the surface of 72 benign and 71 malignant nodules was not stated. In only three cases was the presence of a sharp edge mentioned, and in two of these the nodule was benign. Stony induration, usually considered almost pathognomonic of malignancy, was present in 75 benign nodules, and in none of these cases were calculi demonstrable by roentgenograms. When a calculus could be demonstrated preoperatively, the case was excluded from the series (fig. 2). Stony hard induration was present in 57 malignant nodules and less than stony hard induration in 31 benign and 4 malignant nodules; the amount of induration was not stated for 2 benign and 42 malignant nodules.

The pathological nature of the 108 benign nodules was as follows: benign prostatic hyperplasia, 52; hyperplasia with prostatitis, 24; prostatitis alone, 13; calculi not roentgenographically demonstrable, 6; tuberculosis, 5; normal prostate, 3; infarct, 2; granulomatous prostatitis, 2; and squamous metaplasia, one. In only one of these 108 cases was carcinoma known to have developed some years later, but it was unrelated to the original nodule. The advantage of obtaining exposure of the entire posterior surface of the prostate by the perineal approach lies in the accuracy with which the area under suspicion can be identified and excised for biopsy.

In the group of 103 grossly localized malignant nodules, histological examination of each specimen removed by radical perineal prostatectomy showed that the extent of the cancer had been underestimated to some degree in 74 cases (72%), even after careful rectal palpation. In 26 of these cases, or 25% of the malignant group, tumor cells had unexpectedly invaded the tissues around the seminal vesicles. These figures emphasize the danger of "watchful waiting" in cases of malignancy before undertaking curative surgery.

Perivesicular infiltration by cancer cells was found to be of serious prognostic significance. From 1905 to 1945, 40 patients with localized malignant nodules survived radical perineal prostatectomy and received no precautionary endocrine treatment. In 14 cases the seminal vesicles were involved. Ten of these patients died with cancer; one is still living with cancer. Two died in less than 10 years without cancer, and only one has lived longer than 10 years without recurrence or metas-

From the James Buchanan Brady Urological Institute, Johns Hopkins Hospital.

Read in the Symposium on Some Aspects of Prostatic Cancer before the Section on Urology at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 8, 1955.

1. Jewett, H. J.: Radical Perineal Prostatectomy for Carcinoma: An Analysis of Cases at the Johns Hopkins Hospital, 1904-1954, J. A. M. A. **156**: 1039-1041 (Nov. 13) 1954.

tasis. In 26 of these 40 cases the seminal vesicles were found not to be involved on histological study. Four of these patients died with cancer; one is still living with cancer and assisted with endocrine therapy. Eight died in less than 10 years without cancer, and 13 (50%) lived 10 years or longer without evidence of malignant disease. These figures indicate that microscopic infiltration of the perivesicular tissues markedly reduces the chances for cure. The gross size of the malignant nodule is of less prognostic significance than its histological confinement within the prostate gland.

In the total group of 103 malignant nodules, 77 cases (75%) showed no microscopic evidence of involvement of the seminal vesicles. In this group the nodule was grossly confined to the apex in 22, to the base in 10, and to the center of one lobe in 9. In the remaining 36 cases the position of the nodule was not defined, and it was merely said to be "localized." Definite conclusions therefore cannot be drawn concerning the prognostic significance of the position of the nodule, but it seems obvious that the greater the distance from the nodule to the seminal vesicles the less likely the latter are to be involved.

In the series herein reported, physicians detected 57% more localized malignant nodules during the last decade than during the preceding four decades. In spite of this encouraging trend, the Federal Security Agency, U. S. Public Health Service, reported in 1952 that the incidence of prostatic cancer had increased 38% between 1938 and 1948.[2] Their survey of cancer illness in men also showed that the mortality rate from prostatic cancer was exceeded only by that from cancer of the stomach and lung. Since prostatic cancer is within easy reach of the examining finger and generally commences as a small,

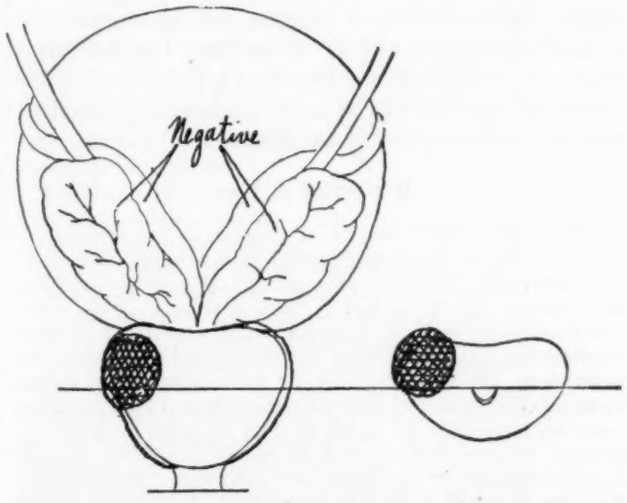

Fig. 1.—Findings on rectal palpation. Nodule of adenocarcinoma localized to base of left lateral lobe of prostate. Radical perineal prostatectomy done Nov. 18, 1935. Patient alive without evidence of recurrence or metastasis and with perfect urinary control 19½ years later.

operable cancer, the responsibility of the general practitioner for the early detection of this disease, in a curable stage, is plainly evident.

Summary and Conclusions

A palpable nodule of abnormal induration localized to a portion of the prostate gland is malignant in about 50% of men over 40 years of age in whom the roentgenogram fails to disclose a calculus. Early detection, through routine annual rectal palpation, becomes the responsibility of the family physician. There are no gross characteristics that are consistently reliable for distinguishing nodules that are benign from those that are malignant. Exposure of the entire posterior surface of the prostate gland by the perineal approach affords the greatest accuracy in identification and excision of the indurated portion for histological examination. It also enables the operator to avoid spillage and implantation of cancer cells and permits a thorough coagulation of the area from which the biopsy specimen is taken. The results of endocrine therapy for indurated prostatic nodules cannot be evaluated without prior histological proof of malignant disease in the patient, inasmuch as approximately 50% of these lesions are benign.

When the nodule is malignant, infiltration of the tissues about the seminal vesicles markedly reduces the prospect for cure by radical prostatectomy. The greater the distance between the nodule and the seminal vesicles, the less likely they are to be involved. The size of the palpable malignant nodule is of less prognostic significance than the histological localization of the neoplasm to the prostate gland itself, in which case the 10-year survival rate is 50% after radical perineal prostatectomy. This survival rate figure of 50% has been found to compare favorably with the expected survivorship of 53% for men of the same age group in the general population.

Fig. 2.—Plain roentgenogram of prostatic area showing compact calculus lying behind right pubis. Rectal palpation had disclosed hard localized nodule in right lobe of prostate.

1201 N. Calvert St. (2).

2. Cutter, S. J., and Marcus, S. C.: Cancer Illness Among Residents of Philadelphia, Pa., 1948, Cancer Morbidity Series, no. 10, Federal Security Agency, U. S. Public Health Service, 1952.

HEMORRHAGIC DIATHESIS IN PATIENTS WITH CARCINOMA OF PROSTATE

George R. Prout, M.D., Malcolm Siegel, Ph.D., Eugene E. Cliffton, M.D.
and
Willet F. Whitmore Jr., M.D., New York

• *An elderly man underwent a transurethral prostatectomy necessitated by carcinoma of the prostate. A year later he returned to the hospital with widespread metastases, pain in the lower extremities, and severe anemia. Ecchymoses present at admission were followed by frank gingival hemorrhages.*

The clotting time of his blood exceeded 30 minutes, and efforts to determine the exact nature of this hemorrhagic diathesis were made by determining the fibrinogen content, semenolytic activity, caseinolytic activity, and other properties of the blood. No simple explanation was found.

The patient's fibrinogen level was twice raised temporarily by intravenous administration of about 5 gm. of human fibrinogen in 1% solution, but it was not affected by diethylstilbestrol diphosphate intravenously, by ethinyl estradiol, by cortisone, or by antihemophilic plasma.

At autopsy, neither the liver nor the spleen showed abnormalities, but the bone marrow generally was replaced by hard, gray homogeneous matter.

It is now well established that metastatic carcinoma of the prostate may be responsible for myelofibrosis, myelopathic anemia, extramedullar hematopoiesis, fibrinolysis, hypofibrinogenemia and hypoprothrombinemia. Cases of involvement of bone marrow and disorders of hematopoiesis alone and other cases of defects in one or more of the clotting factors of blood have been reported (table 1). In view of the pathological processes involved, there is no reason why all cannot occur together.

Rundles and Jonsson [1] studied bone marrow biopsy specimens of 30 patients with carcinoma of the prostate and found neoplastic cells in 17. They and Commons and Strauss [2] reported improvement in the anemia and a decrease in the number of neoplastic cells after castration and hormone therapy. Myhre and Flink [3] reported one case of myelofibrosis and osteosclerosis in which there was unquestionable myelopathic anemia. Weber [4] reported a similar case in which epistaxis, gingival bleeding, and other hemorrhagic phenomena were noted in addition to immature peripheral blood cells seen on smear and an opaque condition of the bones seen on roentgenograms. O'Crowley and co-workers [5] reported on two patients with osteosclerotic metastases and extramedullary hematopoiesis without evidence of myelopathic anemia. Bersack and Feinstein [6] reported a classic case of myelofibrosis in which there were ivory-dense long bones and ribs and marked eburnation of the femurs and tibias. This patient also had myelopathic anemia but, aside from hematuria, experienced no bleeding. Hypofibrinogenemia has been described independent of the other defects by Jurgens and Trautwein [7] and Searle and co-workers.[8] Tagnon and co-workers [9] described the occurrence of fibrinolysis, hypofibrinogenemia, and hypoprothrombinemia in a patient and demonstrated a relationship between androgenic stimulation and the occurrence of these disorders.

Report of A Case

The patient underwent a transurethral prostatectomy in October, 1953, at Bellevue Hospital. A histological diagnosis of carcinoma of the prostate was made, and a bloodless orchiectomy was carried out by occluding both spermatic cords without benefit of a skin incision. Tubercle bacilli were found on sputum examination, and the patient was discharged to a tuberculosis sanatorium. On Sept. 15, 1954, he was readmitted to Bellevue Hospital complaining of severe bilateral leg and knee pain. Aside from nocturia once or twice, he had no other urologic complaints. Examination revealed an elderly, cachectic man with arthritic changes in the hands and right knee. Ecchymoses of the right posterior chest wall were noted. Neither the liver nor the spleen was felt. Roentgenologic survey revealed widespread bone metastases. The hemoglobin level was 9 gm. per 100 ml., and the white blood cell count was 9,600 per cubic millimeter. Urinalysis revealed 1+ albumin, 1+ glucose, and 10 red and 5 white blood cells per high-power field.

One week after admission there was a sudden onset of bleeding from the gingivae. Bleeding time was 30 minutes, prothrombin time was 32 seconds, and the plasma protein level was 5.9 gm. per 100 ml. The serum acid phosphatase level was 0.5 units and serum alkaline phosphatase level 8.3 units. The levels of serum phosphate, cholesterol, and cholesterol esters were normal, as were clotting time and tourniquet test. The bleeding persisted, and, because of a very low plasma fibrinogen level (3 mg. per 100 ml.), he was given 5.5 gm. of that substance

From the Urologic Service of the Department of Surgery and the Andre and Bella Myer Physiology Laboratory, Division of Experimental Surgery, Sloan-Kettering Institute, Memorial Center for Cancer and Allied Diseases. Dr. Prout is Ruth Newman Van Horn Fellow in Surgery (Urology).

Read in the Symposium on Some Aspects of Prostatic Cancer before the Section on Urology at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 8, 1955.

Dr. John W. Draper, Chief of Urology, Cornell Division, Bellevue Hospital, gave permission for study of the patient in the case reported.

The diethylstilbestrol diphosphate used in this study was supplied through Dr. L. A. Crandall of the Miles-Ames Research Laboratories, Elkhart, Ind.

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Studies in the abnormalities of the prothrombin complex were done by Miss Lorraine Herzig in the laboratory of Dr. Irving Wright, New York Hospital–Cornell Medical Center.

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intravenously. The obvious hemorrhage ceased after this treatmen but recurred after 12 hours. Bleeding time was more than 30 minutes during the period when the patient was free from spontaneous hemorrhages. Because of continued bleeding, the patient was transferred to Memorial Center for Cancer and Allied Diseases for further study.

TABLE 1.—*Hemorrhagic Diathesis in Metastatic Carcinoma of the Prostate*

Disorders Caused by Invasion of Marrow
Myelopathic anemia
Irregularity of red blood cell size and shape
Nucleated red blood cells
Thrombocytopenia
Granulocytopenia
Myelofibrosis and osteosclerosis
Extramedullary hematopoiesis
Disorders Caused by Circulating "Semenolysin"
Fibrinolysin
Hypofibrinogenemia or afibrinogenemia
Hypoprothrombinemia
Ac-globulin (factor 5) deficiency
Proconvertin (factor 7) deficiency?

Upon arrival he was feeble, weak, and confused but cooperative; he had huge ecchymoses scattered over his entire body. Crusts of black, dried blood coated his lips and tongue. His blood pressure was 88/58 mm. Hg, pulse 100 beats per minute, and respirations 24 per minute. The scleras had an icteric tint. No nuchal rigidity was present. Generalized muscle wasting was present. Forearm veins were distended, and venous distention of the lower abdominal and lateral thoracic walls could be seen. Increased tactile fremitus, abnormal breath sounds, and rales were present over the upper chest. Examination of the heart was unremarkable. In the abdomen the liver edge, sharp and tender, was palpable three fingerbreadths below the right costal margin. The spleen could not be felt. A large, hard, fixed mass could be felt occupying the right inguinal area and extending above the level of the right inguinal ligament into the pelvis. The scrotal skin was edematous. The testes were felt to be small and firm. Nodularity of the vasa was felt. Rectal examination revealed scanty, stony hard prostatic remnants, above which could be felt several hard, confluent nodules in the region of the seminal vesicles. The right thigh was 5 in. larger than the left as a result of localized edema. Pitting edema there and at the sacral and lumbar areas was also noted.

Admission blood studies revealed a hemoglobin level of 5.4 gm. per 100 ml., 2,200,000 red blood cells per cubic millimeter, a hematocrit of 18, and a white blood cell count of 9,200 per cubic millimeter. Platelet count was 15,000 per cubic millimeter, the clotting time was three hours, and the bleeding time was 5 minutes and 25 seconds. After the patient received 1,000 cc. of packed red blood cells, the hemoglobin level rose to 10.8 gm. per 100 ml. of blood, the red blood cell count to 3,700,000 per cubic millimeter, and the white blood cell count to 6,700 per cubic millimeter. The peripheral blood cell smear at this time revealed an abnormally large number of young red and white blood cells and slight anisocytosis, achromatic poikilocytosis, and polychromatophilia. The bleeding time was 2 minutes and 15 seconds, the clotting time still over 30 minutes, and the platelet count 33,000 per cubic millimeter. The initial urinalysis revealed a specific gravity of 1.010 a faint trace of albumin, and 40 to 60 red blood cells per high-power field. Blood chemistry studies made during the first 48 hours gave the following results: blood urea nitrogen 96 mg. per 100 ml., carbon-dioxide combining power 17 mM. per liter, sodium 136 mEq. per liter, potassium 4.91 mEq. per liter, chloride 95 mEq. per liter, inorganic phosphorus 3.9 mg. per 100 ml., cephalin flocculation 3+ in 48 hours, bilirubin 0.83 mg. per 100 ml., plasma proteins 6.1 gm. per 100 ml., albumin 3.7 gm. per 100 ml., and prothrombin time 26.3 seconds. The alkaline phosphatase level was subsequently reported as 5.5 units and the acid phosphatase level as 0.69 units. The latter rose to 1.07 units one time but was otherwise normal throughout the hospital course. X-rays of the chest, pelvis, and extremities revealed widespread osteolytic and osteoblastic lesions.

The patient received diethylstilbestrol diphosphate, 750 mg. intravenously five days before transfer and again on arrival at Memorial Center, then 500 mg. daily intravenously for eight days after admission (table 2, fig. 1). Therapy with ethinyl estradiol, 1 mg., was then started and given daily until the patient's death. Therapy with cortisone acetate, 100 mg. three times daily, was begun on Oct. 29, and the dosage was subsequently decreased to 100 mg. each day. Calcium chloride and meralluride injection U. S. P. were used in an effort to decrease massive edema, but with little effect. The patient was not given transfusions of whole blood until Oct. 25. Subsequently, he received transfusions and antihemophilic plasma. On Nov. 4 he received 500 ml. of fresh blood that had been collected in a nonwettable container and 500 ml. of day-old blood collected in the usual manner. Human fibrinogen, supplied by the American Red Cross, was given on Oct. 14 (4.4 gm.) and on Oct. 19 (2.2 gm.). Clinical improvement was evident for a few hours after the fibrinogen had been given, but persistent oozing from sites of previous venipunctures, gingivae, and tongue soon recurred. Despite therapy, the patient died on the 28th day.

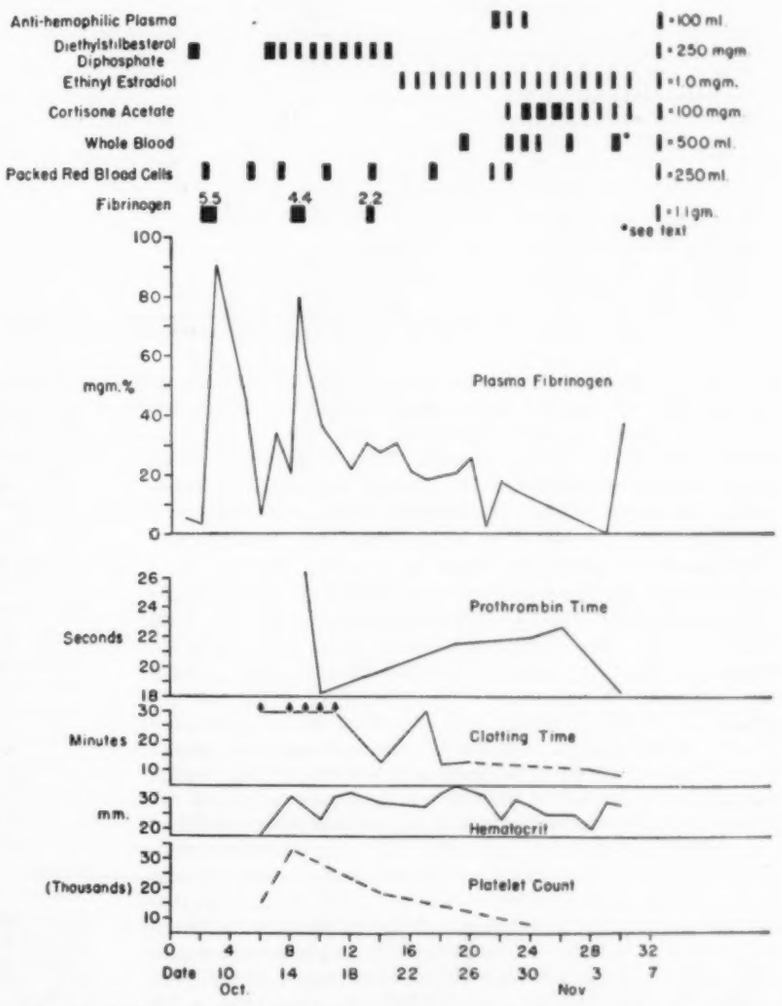

Fig. 1.—Effect of therapeutic modalities on fibrinogen levels in hemorrhagic diathesis from metastatic carcinoma of prostate.

Autopsy Findings.—Extensive ecchymoses of the entire body and dark, bloody material in the nose and mouth were evident. The mass in the right inguinal region was found to be firmly attached to the deeper posterior structures. When the abdominal cavity was opened, the pelvic viscera were found to be incorporated in a large, nodular mass invading the bladder wall,

prostatic bed, and seminal vesicles. The mass extended from the prostate to the right side of the pelvis, destroying large portions of the right ilium, sacrum, and pubis. There were bilateral fibrotic adhesions of the pleura and a 3-cm. healed tuberculous lesion at the apex of the right lung. In the heart, arteriosclerotic changes and an irregular, reddish-gray area on the posterior wall of the left ventricle were noted. Hydroureter and hydronephrosis were present on the right due to obstruction by the pelvic mass. The left kidney and ureter were unremarkable. Bone marrow was replaced by hard, gray homogeneous matter. Subarachnoid hemorrhage in the left parietal lobe of the brain was seen. Stomach, liver, gallbladder, spleen, neck organs, pancreas, and gastrointestinal tract showed no abnormalities nor hemorrhage. In the ventricular wall a recent infarction was noted. The lungs, in addition to healed tuberculosis, revealed bronchopneumonia and metastatic carcinoma filling the endothelial lining spaces. The tracheobronchial lymph nodes revealed metastatic carcinoma. In the kidney, metastatic calcific deposits were noted in the tubules and colonies of bacteria were seen in the glomeruli. Many of the tubules revealed degeneration of the epithelium and hyaline and hemoglobin casts. Infiltration of the entire vesical wall and ureteric walls was seen. The marrow showed extensive replacement with tumor tissue, and the brain, subarachnoidal and cortical hemorrhage. Pelvic mass sections showed anaplastic prostatic carcinoma with blood vessel, lymphatic, and nerve bundle invasion. Final diagnoses included anaplastic adenocarcinoma of the prostate with extensive metastases, myocardial infarct, bronchopneumonia, infarcted testes, healed pulmonary tuberculosis, and hemoglobinuric nephrosis.

Laboratory Studies.—On a few occasions the patient's blood failed to clot. On every occasion that clotting did occur the clot disappeared in less than 24 hours when incubated at 37 C. Most frequently the clot disappeared within eight hours, and on several occasions it disappeared in less than an hour without incubation. To determine the fibrinolytic effect of the patient's plasma, a standard bovine clot was used as a substrate.[10] Plasma, serum, and the euglobin fraction in amounts no greater than 0.1 ml. were studied for spontaneous activity. Even though the fibrinogen content of the clot was decreased on several occasions, no spontaneous fibrinolytic activity was observed. When the patient's plasma was activated with streptokinase-streptodornase (Varidase) (a solution in veronal buffer at pH 7.4 containing 10,000 units of streptokinase and 2,000 units of streptodornase in each milliliter), lysis of the bovine clot occurred (table 3). One milliliter of the patient's fresh plasma was mixed with 4 ml. of normal, freshly drawn whole blood on the dates mentioned below. The resultant clot failed to lyse on Oct. 8, 25, and 30 but did lyse on Oct. 14, 16, and 27. The same donor's blood was clotted with normal plasma from a second donor as a control. On Oct. 25, the control's blood failed to clot, but on every other occasion the contents of both tubes clotted simultaneously. The control clot never lysed. On Oct. 16, 0.25 ml. of the patient's fresh plasma was clotted with 0.1 ml. of bovine thrombin in the presence of 1 ml. of 0.2% human fraction 1. A control substituting normal, fresh plasma was set up. No lysis was present in either tube in 24 hours. In the tube in which the patient's plasma of that day and 4 ml. of fresh whole blood had been clotted together, lysis occurred in 90 minutes. The corresponding control failed to lyse (table 4, fig. 2 *center* and *bottom*).

Fibrinogen content [11] was determined immediately after venipuncture, and the plasma was then incubated for 24 hours at 37 C. The values remained essentially the same (table 5). The fibrinogen content was determined in the patient's fresh plasma on the following day at the same time that the determination was carried out on the incubated specimen. Since there was a lack of human fibrinogen in sufficient quantities, 0.5 ml. of the patient's plasma collected on Oct. 26 and 2 ml. of normal plasma were added together. Fibrinogen determinations at 0 hours and 24 hours were, for practical purposes, the same. With use of the patient's plasma (Oct. 7) that had been frozen for 18 hours, 0.2 ml. was placed in each of five tubes to which was added 0.15 ml. of a 1% bovine fibrinogen solution,[10] and veronal buffer at pH 7.4 was added to bring the volume to 0.9 ml. At intervals from 4 to 150 minutes, 0.1 ml. of thrombin was added. The contents of all tubes clotted promptly and firmly after thrombin was added (table 6). On Oct. 8, the same technique with 0.2 ml. and 0.4 ml. of the patient's fresh plasma was used, but no clot was formed with the addition of thrombin after 24 hours of incubation at 37 C. We failed to have proper control studies on this date, however. The experiment was repeated on Oct. 16; elevation in the clotting time was unquestionable. On several occasions we attempted to reduplicate these observations, but the data are so inconstant that interpretation is not possible.

With use of a modification of the method described by Downie and Cliffton,[12] a 5% casein solution was incubated 14 hours at 37 C with either 1 ml. of the patient's plasma or 1 ml. of the patient's serum. Both were obtained and used Oct. 18. No tyrosine was released. With use of 0.8 ml. of the euglobulin fraction of the thawed plasma of Oct. 13, 0.2 ml. of streptokinase-streptodornase, and the same casein solution, incubation for 22 hours produced 45 mcg. of tyrosine (table 7) per hour. This experiment was performed repeatedly with the same results.

Several studies were made on the abnormalities in the clotting mechanisms of the patient. Determination of the usual prothrombin time and the dilute prothrombin time revealed pronounced deficiencies in the total and the prothrombin complex. The quantity of Ac-globulin (factor 5) was determined and found to be decreased only once. The amount of proconvertin (factor 7) was consistently decreased, prothrombin test showed no consumption, recalcification time was prolonged, and no abnormality in the antithrombin titer was found (table 8).

TABLE 2.—*Data on Therapy and Tests over Thirty-*

Therapy or Test	7	8	9	10	11	12	13	14	15	16	17	18
Antihemophilic plasma, ml.	...	...	...	...	...	...	...	...	...	...	...	...
Diethylstilbestrol diphosphate, mg. (I.V.)	750	...	...	...	...	750	500	500	500	500	500	500
Ethinyl estradiol, mg.	...	...	...	...	...	...	...	...	...	...	...	...
Cortisone acetate, mg. (I.M.)	...	...	...	...	...	...	...	...	...	...	...	...
Human fibrinogen, 1.1% solution (I.V.)	...	5.5 gm.	...	...	...	...	...	4.4 gm.	...	...	...	...
Whole blood, ml.	...	...	...	...	...	...	...	...	...	...	...	...
Packed red blood cells, ml.	...	500	...	...	500	...	500	...	...	500	...	...
Plasma fibrinogen determinations, mg.	5	3	90	...	45	6	33	8 a. m. 20 2 p. m. 79	59	36	29	21
Prothrombin time, seconds	...	...	...	...	...	...	...	...	26.3	18.2	...	...
Clotting time, min.	...	...	...	...	...	30↑	...	30↑	30↑	30↑	30	...
Hematocrit, mm.	...	...	...	...	...	18	25	31	27	23	31	32
Platelet count, thousands	...	...	...	...	...	15	...	33	...	...	...	...

* 500 ml. of 24-hr. old bottled blood; 500 ml. of fresh blood, nonwettable container.

10. Cliffton, E. E., and Cannamela, D. A.: Fibrinolytic and Proteolytic Activity of a "Human Plasminogen," Prepared from Fraction III of Human Plasma, J. Appl. Physiol. **6**: 42, 1953.

11. Parfentjev, I. A.; Johnson, M. L., and Cliffton, E. E.: The Determination of Plasma Fibrinogen by Turbidity with Ammonium Sulfate, Arch. Biochem. **46**: 470, 1953.

12. Downie, G. R., and Cliffton, E. E.: A Method for Assay of Serum Proteolytic Activity, Proc. Soc. Exper. Biol. & Med. **71**: 138, 1949.

Comment

Huggins and others [13] demonstrated a wide species difference in the prostatic fluid of mammals. They showed the most prominent proteolytic activity in human prostatic fluid to be fibrinolytic, though enzymatic activity with hemoglobin could be demonstrated. Tagnon and others [14] have shown that carcinomatous prostatic tissue extract has fibrinolytic activity against a bovine fibrin clot tagged with radioactive iodine. The extract also produced prolonged prothrombin time in vitro. The addition of Ac-globulin corrected this.

Using a bovine fibrinogen-thrombin clot we attempted to show spontaneous fibrinolytic activity by this patient's plasma. We were unable to do so (table 3) in spite of the obvious hemorrhagic diathesis. Fibrinolytic activity against a bovine clot could be demonstrated only when streptokinase-streptodornase was added. A normal amount of plasmin activity was then demonstrated, indicating that the plasminogen-plasmin system was probably not responsible for the hemorrhagic diathesis. It is possible that we failed to add enough plasma and euglobin fraction or that the activity does not lie in the euglobin fraction. This patient's fibrinogen and platelet levels were very low, and it seemed reasonable to postulate that the fibrin mesh was scanty and that, as clot retraction occurred, the red blood cells slipped out and the remaining small, fragile mesh was then lost or easily broken up. When we first mixed the patient's plasma and normal blood, no lysis occurred. On three ensuing occasions we found that lysis of the resultant clot occurred. On one occasion the patient's plasma was clotted with human fraction 1 by the addition of bovine thrombin, while the same plasma was clotted with freshly drawn normal blood. Lysis occurred only in the tube in which the patient's plasma was clotted with whole blood (fig. 2, table 4). We performed this particular experiment with fraction 1 only once. It is unlikely that the fraction 1 employed had an antiproteolytic contaminant because antiproteolytic activity is associated with the albumin fraction. Not considering the unlikely possibility that a species difference in substrate materially alters the activity of the enzyme in question, it is interesting that the positive results occurred when blood clotted in the presence of the patient's plasma, whether in vivo or in vitro. Though no conclusion can be drawn, this suggests that the actual clotting of whole blood may in some way activate the enzyme.

We have included some of our studies on fibrinogen destruction not because they constitute incontrovertible

Day Period in a Patient with Hemorrhagic Diathesis

October													November				
19	20	21	22	23	24	25	26	27	28	29	30	31	1	2	3	4	5
...	...	...	...	...	...	...	...	200	100	100	...	...	...	...	...	...	...
500	500	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	...	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
...	...	...	...	...	...	...	...	...	100	300	300	300	200	200	100	100	100
2.2 gm.	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
...	...	...	...	...	...	1,000	...	...	1,000	1,000	500	...	500	...	...	1,000*	...
500	...	...	...	500	...	...	...	250	500	...	...	...	...	...	...	...	...
30	27	30	20	18	...	20	25	2	17	14	...	...	7	...	...	0	37
19.3	...	...	...	...	...	21.5	...	...	...	...	21.9	...	22.6	...	...	...	18.3
...	12.5	...	...	30	12	...	12.5	...	...	...	...	...	...	...	10	...	8
...	29	...	...	27	32	35	...	31	23	30	28	25	...	25	20	29	28
...	18.5	...	...	...	...	...	...	...	...	...	8	...	...	...	...	...	...

TABLE 3.— *Plasma and Euglobin Fraction "Semenolytic" Studies on Standard Bovine Clot*

Blood Drawn, Experiment Done 10/14/54	Volume Added (Ml.)					Min. Necessary to Lyse Clot Formed			
	Sample	Veronal Buffer pH 7.4	Streptokinase-Streptodornase	Fibrinogen (1%)	Thrombin	1	2		60
Euglobin	0.10	0.65	....	0.15	0.10	.....	.....	→	No lysis
	0.05	0.70	....	0.15	0.10	.....	.....	→	No lysis
	0.01	0.74	....	....	0.10	.....	.....	.....	
Euglobin activated	0.10	0.55	0.10	0.15	0.10	→	Lysed	.....	
	0.05	0.60	0.10	0.15	0.10	→	Lysed	.....	
	0.01	0.64	0.10	0.15	0.10	→	Lysed	.....	
Plasma	0.10	0.65	....	0.15	0.10	.....	.....	→	No lysis
	0.05	0.70	....	0.15	0.10	.....	.....	→	No lysis
	0.01	0.74	....	0.15	0.10	.....	.....	→	No lysis
Plasma activated	0.10	0.55	0.10	0.15	0.10	→	Lysed	.....	
	0.05	0.60	0.10	0.15	0.10	→	Lysed	.....	
	0.10	0.64	0.10	0.15	0.10	→	Lysed	.....	
Control A	....	0.65	0.10	0.15	0.10	.....	.....	→	No lysis
Control B	....	0.75	....	0.15	0.10	.....	.....	→	No lysis

13. Huggins, C., and Vail, V. C.: Plasma Coagulation and Fibrinogenolysis by Prostatic Fluid and Trypsin, Am. J. Physiol. **139**: 129, 1943. Huggins, C., and Neal, W.: Coagulation and Liquefaction of Semen: Proteolytic Enzymes and Citrate in Prostatic Fluid, J. Exper. Med. **76**: 527, 1942.

14. (*a*) Tagnon, H. J.; Whitmore, W. F., Jr.; Schulman, P., and Kravitz, S. C.: The Significance of Fibrinolysis Occurring in Patients with Metastatic Cancer of the Prostate, Cancer **6**: 63, 1953. (*b*) Footnote 9.

evidence but to mention a few of the many studies that defied interpretation (tables 5 and 6). Reasoning that lysis of a normal clot represents evidence of potent digestion of fibrin, one might expect demonstrable fibrinogenolytic activity in the patient's plasma (table 5). A significant fall in fibrinogen content did not occur. It is not surprising, however, that the fibrinogen content failed to fall when normal plasma and the patient's plasma were mixed. This lack of fibrinogenolytic activity is possibly

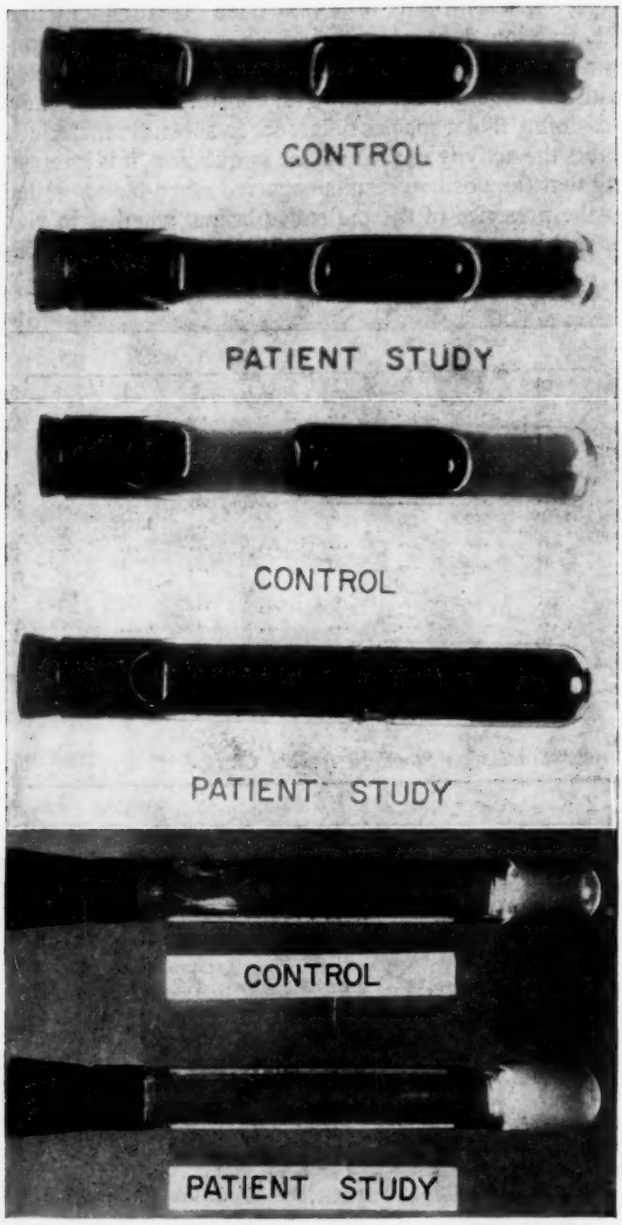

Fig. 2.—*Top*, two clot studies done Oct. 8, with no lysis. *Center*, studies done Oct. 16, with lysis in 90 minutes. *Bottom*, patient's plasma of Oct. 16, human fraction 1, and thrombin. No lysis occurred.

due to antiproteolytic activity in the normal plasma. This thesis seems inadequate, since lysis of a normal clot was demonstrated on several occasions. The explanation probably lies in two factors. First, human prostatic fluid has been demonstrated to have greater activity against fibrin than any other substrate. Since the same situation may be expected for a proteolytic enzyme of prostatic origin in plasma, the antiproteolytic activity present in normal plasma may block the weaker fibrinogenolytic activity of the enzyme. Secondly, the act of clotting allows closer contact of enzyme and substrate; hence, the enzyme would appear to digest fibrin selectively.

On at least one occasion we demonstrated prolongation of the clotting time after incubation of the patient's plasma with fibrinogen. This we consider the result of

TABLE 4.—*Two-Clot Study for "Semenolysis"*

	Time for Lysis to Occur
Patient study 1 (fresh plasma of 10/16) 1 ml. of patient's plasma 4 ml. of donor A blood	Lysis in 90 min.
Patient study 2 0.25 ml. of patient's plasma 1.0 ml. of human fraction 1 (0.2%) 0.1 ml. of thrombin	Still clotted in 24 hr.
Control 1 (fresh plasma of 10/16) 1 ml. of donor B plasma 4 ml. of donor A blood	Still clotted in 24 hr.
Control 2 0.25 ml. of donor B plasma 0.1 ml. of human fraction 1 (0.2%) 0.1 ml. of thrombin	Still clotted in 24 hr.

fibrinogen digestion alone, since all other factors were supplied (table 6). Caseinolytic activity in the patient's plasma was not shown until plasminogen was activated by streptokinase-streptodornase (table 7).

Since the physiological function of the enzyme under discussion is apparently to lyse clotted semen, this activity may be termed "semenolytic." Because of the numerous frequently confusing terms applied to proteolytic enzymes and their functions, we propose that the proteolytic activity associated with decreased fibrinogen level, elevated prothrombin time, and defects in the prothrombin complex in the presence of metastatic carcinoma of the prostate be termed "semenolysis" and the enzyme "semenolysin."

Of considerable interest are the reports we received on the abnormalities in clotting mechanism (table 8). Both the usual and the dilute (12.5% plasma) prothrombin times were always elevated. Studies on specific factors revealed a decrease in proconvertin on three occasions. Tagnon and others [14a] have shown that the amount of Ac-globulin is decreased on incubation with the plasma of a patient suffering from metastatic carcinoma of the prostate. Another patient, reported on by Cosgriff and Leifer [15] had a pronounced Ac-globulin deficiency, probably on the basis of semenolysis. On two occasions, by a qualitative test, the Ac-globulin was normal in the patient whose case is presented; on a third, it was decreased. No effort was made to quantitate this reduction. These determinations suggest that digestion by the circulating

TABLE 5.—*Fibrinogen Determinations After Incubation of Patient's Plasma**

Date, October	Fresh Plasma Fibrinogen, Mg. per 100 Ml.	Incubated Plasma Fibrinogen, Mg. per 100 Ml.
19	29	29
20	27	..
25	20	18
26	25	..

* 24 hr. at 37 C.

semenolysin is variable, a fact that might be anticipated in view of the complex kinetics of enzyme systems and the variability in production and life span of the substrates involved. The clotting, bleeding, and recalcification times and the prothrombin consumption test require no special comment.

Diagnosis and Therapy

Given an individual with symptoms and signs of carcinoma of the prostate who has ecchymotic areas or frank hemorrhage, the diagnostic measures necessary to establish the cause are few and can be carried out in a brief period of time in most institutions. If x-rays of the bones reveal metastases and phosphatase determinations are abnormal, there is strong evidence that metastatic carcinoma of the prostate is present. Myelopathic anemia can be determined by a complete blood cell count and a platelet count. Clotting time may be normal and only the bleeding time elevated if myelopathic anemia is present. Even if young blood cell forms, severe anemia, and thrombocytopenia are present, prothrombin time and, if possible, fibrinogen level should be determined, since

TABLE 6.—*Plasma Studies for Semenolytic Activity with Fibrinogen*

Patient's Plasma, Ml.	Veronal Buffer, Ml.	Fibrinogen, Ml.	Thrombin, Ml.	Clotted at	Lysis in 24 Hr.
10/7/54					
0.2	0.5	0.15	0.1	4 min.	Not read
0.2	0.5	0.15	0.1	13 min.	Not read
0.2	0.5	0.15	0.1	30 min.	Not read
0.2	0.5	0.15	0.1	60 min.	Not read
0.2	0.5	0.15	0.1	150 min.	Not read
0.5	0.25	0.15	0.1	Immediately	—
0.2	0.65	0.15	0.1	Immediately	—
—	0.75	0.15	0.1	Immediately	+
10/8/54					
0.4	0.35	0.15	0.1*	No clot on the addition of thrombin 24 hr later	
0.2	0.55	0.15	0.1*		
10/16/54					
0.2	0.55	0.15	0.1	Immediately	Clotting time 24 hr. later (Still clotted)
—	0.75	0.15	0.1*		9 seconds
0.2	0.55	0.15	0.1*		28 seconds
0.4	0.35	0.15	0.1*		23 seconds
0.2	0.55	0.15*	0.1*		9 seconds
Normal Plasma 10/16/54					
0.2	0.55	0.15	0.1	Immediately	(Still clotted)
0.2	0.55	0.15*	0.1*		9 seconds
0.2	0.55	0.15	0.1*		6 seconds
0.4	0.35	0.15	0.1*		6 seconds

* Added 24 hr. later.

semenolytic activity may accompany bone marrow invasion. Though the patient's clot may lyse, this phenomenon is not necessarily the *sine qua non* of semenolytic activity. The injection of mercurial diuretics, hemorrhagic shock, acute trauma, and periods of anoxemia can produce spontaneous fibrinolysis. We have seen a patient with acute myelocytic leukemia with a low fibrinogen level whose clot disappeared on incubation. Overzealous agitation at observation may also produce apparent lysis.

In the absence of severe liver disease with evidence of metastatic carcinoma of the prostate, an elevated prothrombin time and a decrease in the fibrinogen level should make one suspect that semenolytic activity is present. If prothrombin and fibrinogen levels are normal, there is scant possibility that semenolysis is present. Once semenolytic activity in the blood is suspected, therapy with feminizing hormones should be instituted immediately. Myelopathic anemia will also respond to this therapy. Once bleeding has been controlled, steps should be taken to substantiate the clinical impression of prostatic malignancy by histological diagnosis. Orchiectomy should be carried out subsequently.

Unfortunately, the hemorrhagic diathesis of carcinoma of the prostate may be a late complication of the disease and occur after the neoplastic process has escaped hormonal control, as in the case that we have presented. In table 2 and figure 1 are shown the effects of various therapeutic modalities on the fibrinogen level

TABLE 7.—*Proteolytic (Caseinolytic) Study Oct. 18, 1954*

		Klett Reading	
A	Experiment Materials Used	2 Min.	14 Hr.
1	Casein, 4.0 ml. Patient's plasma (10/18), 1.0 ml.	96	96
2	Casein, 4.0 ml. Patient's serum (10/18), 1.0 ml.	98	98
3	Veronal buffer, 4.0 ml. Patient's serum (10/18), 1.0 ml.	66	77
4	Veronal buffer, 4.0 ml. Patient's plasma (10/18), 1.0 ml	60	68
B		2 Min.	22 Hr.
1	Casein, 4.0 ml. Buffer, 1.0 ml.	69	72
2	Casein, 4.0 ml. Streptokinase-streptodornase, 0.2 ml. Veronal buffer, 0.8 ml.	67	69
3	Casein, 4.0 ml. Euglobulin (10/13), 0.8 ml. Buffer, 0.2 ml.	69	80
4	Casein, 0.2 ml. Euglobulin (10/13), 0.8 ml. Streptokinase-streptodornase, 0.2 ml.	73*	455*

* Indicating 45 mcg. of tyrosine liberated each hour.

in the plasma. Neither diethylstilbestrol diphosphate given intravenously nor ethinyl estradiol produced any demonstrable effect on the fibrinogen level. Likewise, cortisone acetate caused no alteration in the determinations. The two significant elevations occurred after 5.5 gm. and 4.4 gm. of human fibrinogen had been given as a 1% solution. A smaller dose, 2.2 gm., stopped the precipitous drop, but no abrupt elevation was observed. Antihemophilic plasma was then given, and it too produced no significant peak. We then gave 1 liter of 24-hour old blood. Five hundred milliliters had been collected in a nonwettable container and another 500 ml. in the usual glass container. Since they were given in immediate succession, it is impossible to assess their separate effects, but, collectively, they produced an unquestionable rise in the fibrinogen level.

TABLE 8.—*Prothrombin Complex and Other Studies*

	Oct. 9		Oct. 11		Oct. 14	
Prothrombin Complex Time	Undilute	Dilute	Undilute	Dilute	Undilute	Dilute
Control	14.8	40.2	15.0	40.5	15.5	42.2
Patient	20.7	85.6	24.6	116.8	23.5	139.1
Ac-globulin (factor 5)	Normal		Normal		<Normal	
Proconvertin (factor 7)	65% of normal		65% of normal		65% of normal	
Prothrombin	50% of normal		50% of normal		50% of normal	
Recalcification time*						
Control	2 min. 30 sec.		2 min. 30 sec.		—	
Patient	2 min. 45 sec.		4 min.		Prolonged	
Prothrombin consumption test.	—		—		No consumption	
Antithrombin titer	—		—		Normal	

* Blood was centrifuged for 10 min. at 1,700 rpm.

Crane and co-workers [16] have recently reported two cases of afibrinogenemia associated with carcinoma of the prostate. In one of these spontaneous lytic activity was present. Soy bean inhibitor was given with whole

15. Cosgriff, S. W., and Leifer, E.: Factor 5 Deficiency in Hemorrhagic Diathesis (Parahemophilia), J. A. M. A., **148**: 462 (Feb. 9) 1952.

16. Crane, J. J.; Ware, A. G., and Hamilton, J.: Spontaneous Afibrinogenemia in Cancer of the Prostate, J. Urol. **73**: 379, 1955.

blood to this individual, and bleeding ceased. We used a 0.035% solution of soy bean inhibitor in varying concentrations when studying fibrinogenolytic activity and could demonstrate no interpretable effect on clotting. Our techniques admittedly need refinement, and soy bean inhibitor may actually be of great value in the treatment of semenolytic hemorrhagic diathesis. We did not use it for fear of foreign protein reaction. We did not add soy bean inhibitor to the patient's blood before clotting to determine the presence of antisemenolytic properties.

Scott and others [17] have recently treated five patients with abnormal proteolytic activity in the plasma. Two of these were men undergoing prostatectomy for benign disease. Bleeding during the immediate postoperative period occurred in both, and death resulted in one. Abnormal plasma proteolytic activity was noted and afibrinogenemia was present in the man who died. These authors make no mention of fibrinolytic studies based on lysis of a bovine clot but do mention that the addition of the patient's plasma to a normal human clot produced lysis, as we observed in this case. Since antiproteolytic activity is associated with fraction 5 (the albumin-containing fraction), these authors treated four different types of abnormal plasma proteolytic activity with salt-poor albumin. This therapy may be of great value also. More studies are needed to evaluate its effect. When one is confronted with a similar clinical situation, all forms and types of therapy should be instituted. The prognosis is grave, and, if the patient is in relapse, death due to hemorrhage or cerebral vascular catastrophe is probable.

Summary

Metastatic carcinoma of the prostate may produce hemorrhagic diathesis on the basis of bone marrow invasion or by the production of a proteolytic enzyme arising from prostatic tissue. Both mechanisms may be functioning simultaneously. Deficiencies in fibrinogen, prothrombin, Ac-globulin, and proconvertin may be present if spontaneous enzymatic activity is responsible for the hemorrhage. Spontaneous lysis of the patient's clot and lysis of a clot produced by mixing normal whole blood and the patient's plasma may also be observed; semenolysis, a new term devised to describe this activity has been suggested. Therapy with female hormones and orchiectomy will control the hemorrhagic diathesis if the tumor tissue is sensitive to hormones. If the hemorrhage is on the basis of semenolytic activity, human fibrinogen, fresh whole blood, and antihemophilic plasma will produce a temporary cessation of bleeding.

444 E. 68th St. (21) (Dr. Prout).

17. Scott, E. V. Z.; Matthews, W. F.; Butterworth, C. E., Jr., and Frommeyer, W. B., Jr.: Abnormal Plasma Proteolytic Activity, Surg. Gynec. & Obst. **99**: 679, 1954.

FIBROCYSTIC DISEASE OF THE PANCREAS, A GENERALIZED DISEASE OF EXOCRINE GLANDS

Paul A. di Sant'Agnese, M.D., New York

• *The characteristic lesions of fibrocystic disease in the pancreas involve the exocrine structures, and far-reaching nutritional disturbances follow the loss of the external pancreatic secretion. The endocrine structures remain intact, and the islands of Langerhans continue to produce internal secretion.*

A study of 325 cases showed that the disease is really systemic; it is not limited to the pancreas but involves exocrine glands in many other parts of the body. Focal necrosis with biliary obstruction is seen in the liver, the sweat glands secrete abnormally high concentrations of electrolytes, and in nearly all cases there is pulmonary disease characterized by abnormal production of mucus and obstruction of bronchi.

There were 145 deaths in this series, and 130 were ascribed to the pulmonary involvement. The abnormally high losses of sodium chloride in the sweat during hot weather may also be fatal. Progress in the diagnosis and treatment of this important disease depends on greater recognition of its systemic character and its importance in the pathogenesis of meconium ileus, chronic pulmonary disease, cirrhosis of the liver, and portal hypertension in children.

Fibrocystic disease of the pancreas is a hereditary disease of children in which many and perhaps all exocrine glands are affected. Involvement of the pancreas, lungs, liver, and sweat and salivary glands gives rise to manifold clinical manifestations (table 1). This generalized glandular disorder in the pediatric age group accounts for virtually all cases of pancreatic deficiency, for a majority of those with chronic (nontuberculous) lung disease, and for one-third of the children with cirrhosis of the liver and portal hypertension. Abnormal sweat electrolyte concentration in hot weather may lead to massive salt depletion and death. Fibrocystic disease of the pancreas occurs equally in all groups of Caucasians; it is rare in Negroes and has never been found in Mongolians. Its incidence has been estimated at about 1 in 600 live births. In the 15-year period 1939-1954, 325 patients with this disease were seen at Babies Hospital.

The condition was noted in Switzerland by Fanconi in 1936.[1] The first complete description in this country was given by Andersen in 1938.[2] Attention was first focused on the pancreas, but it was soon realized that severe pulmonary involvement was found to be present in almost all cases.[3] More recently, sweat and salivary

From the Department of Pediatrics, Columbia University College of Physicians and Surgeons, and the Babies Hospital.

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1. Fanconi, G.; Uehlinger, E., and Knauer, C.: Das Coeliakiesyndrom bei angeborener zystischer Pancreasfibromatose und Bronchiektasien, Wien. med. Wchnschr. **86**: 753, 1936.

glands have been shown to be consistently affected in this disease.[4] It is now recognized that characteristic lesions are found in the liver at postmortem examination in one-fourth or more of the cases, which at times lead to manifestations that may dominate the clinical picture.[5] Involvement of mucous glands throughout the body (intestinal, genitourinary tract, and others) is occasionally found at autopsy,[6] but there are no recognized symptoms.

System Involvement and Resulting Symptoms

Pancreas.—The microscopic lesions in the pancreas are striking.[6] Amorphous eosinophilic concretions (assumed to be inspissated abnormal secretions) obstruct the large and small ducts, with consequent dilatation of the acini and degeneration of the parenchyma, which is gradually replaced by fibrous tissue. Infiltration by inflammatory cells is frequently marked. The islands of Langerhans are intact, correlating with the fact that sugar metabolism is unaltered; this is an example of the coexistence in the same location of two tissues different in function and origin. An important pathological feature of the pancreatic lesion is its progressive nature. Initial lesions are present in most instances at birth but become progressively more severe over a period of a few months or two or three years.

Because of the absence of all three pancreatic enzymes —trypsin, amylase, and lipase—foodstuffs are poorly digested and absorbed.[7] Fats are not split, an essential preliminary to intestinal absorption and, consequently, large amounts of neutral fats are found in the stools. A varying, but large, percentage of the liposoluble vitamins A, D, and K are also lost because of the steatorrhea. Protein and, to a smaller extent, carbohydrates are also poorly handled and are found in the feces in large amounts. In contrast to fats, however, protein does no apparent harm if given in large amounts. By increasing the amount of protein foods ingested it is possible therefore to obviate their poor utilization. Simple carbohydrates, monosaccharides and disaccharides, which need almost no processing for intestinal absorption, are well utilized.

Because so much of the ingested food is not absorbed and utilized, malnutrition is frequently marked despite an apparently adequate caloric intake. Typically, the patient, often an infant, is reported not gaining weight despite an excellent appetite and is undernourished and underdeveloped. The muscle tone is usually good, the abdomen is frequently distended, and stools are increased in number (two to five a day) and bulky, greasy, and extremely foul but almost never watery. In most patients, complete pancreatic achylia is present at birth, but in about 10% pancreatic function is still partially preserved or even normal.[8] In such patients symptoms may appear later or remain in abeyance indefinitely. As expected, the abnormal stools, malnutrition, and excessive appetite consequent to deficiency of pancreatic function are mild or entirely absent.

Respiratory Tract.—In almost all 325 patients, pulmonary involvement of varying degree occurred at some time in the course of the illness. In the average case the respiratory disease was severe and accounted for over 90% of the 145 deaths. The paranasal sinuses were also consistently involved in all patients but did not appear in most instances to give rise to serious problems if the lung

TABLE 1.—*Sequence of Events* in Fibrocystic Disease of the Pancreas*

						Other Exocrine Glands			
	Meconium Ileus	Pancreas	Lungs	Sweat Glands	Liver	(Gastric)†	Parotid	Mixed Salivary	Mucus-Producing
Defect	Inspissated meconium	Exocrine pancreatic deficiency	Bronchial obstruction	Abnormally increased sweat electrolytes	Focal fibrosis with biliary obstruction	(Increased electrolytes)	Increased secretory rate	Increased electrolytes	Scattered occasional histological lesions
Symptoms	Intestinal obstruction in newborn infant	Steatorrhea; malnutrition; underdevelopment	Chronic pulmonary disease	Massive salt depletion in hot weather	Cirrhosis; portal hypertension	Dehydration; hypochloremia; metabolic alkalosis	No clinical manifestations	No clinical manifestations	No clinical manifestations
Test indicated	.....	Duodenal assay	X-rays of chest	Sweat test	Physical examination	.....	.....	.....	.....
Results of test	.....	Absent pancreatic enzymes	Obstructive emphysema; chronic bronchopneumonia	High sweat chloride and sodium	Hepatosplenomegaly	.....	.....	.....	.....
Treatment	Surgery	Dietary and substitution therapy	Antibiotic therapy	Intravenously given sodium chloride; increased salt intake	Surgical shunting procedures	Intravenously given fluid therapy	None	None	None

* Basic hereditary defect is unknown. Clinical picture varies according to organ or gland predominantly involved.
† ( ) indicate sequence of events not proved.

2. Andersen, D. H.: Cystic Fibrosis of the Pancreas and Its Relation to Celiac Disease: A Clinical and Pathologic Study, Am. J. Dis. Child. **56**: 344 (Aug.) 1938.

3. Footnotes 1 and 2.

4. (*a*) di Sant'Agnese, P. A.; Darling, R. C.; Perera, G. A., and Shea, E.: Abnormal Electrolyte Composition of Sweat in Cystic Fibrosis of the Pancreas: Clinical Significance and Relationship to the Disease, Pediatrics **12**: 549, 1953. (*b*) di Sant'Agnese, P. A.; Grossman, H., and Darling, R. C.: Involvement of Salivary Glands and Electrolyte Studies of Duodenal Contents in Fibrocystic Disease of the Pancreas, to be published.

5. di Sant'Agnese, P. A., and Blanc, W. A.: Fibrocystic Disease of the Pancreas with Cirrhosis of the Liver and Portal Hypertension, Pediatrics, to be published.

6. (*a*) Footnote 2. (*b*) Farber, S.: Pancreatic Function and Disease in Early Life: V. Pathologic Changes Associated with Pancreatic Insufficiency in Early Life, Arch. Path. **37**: 238 (April) 1944. (*c*) Fibrocystic Disease of the Pancreas: A Congenital Disorder of Mucus Production—Mucosis, Bodian, M., editor, London, England, William Heinemann, Ltd., 1953.

7. (*a*) Footnote 6. (*b*) May, C. D.: Cystic Fibrosis of the Pancreas in Infants and Children, Publication 234, American Lecture Series, Monograph in American Lectures in Pediatrics, Springfield, Ill., Charles C Thomas, Publisher, 1954.

8. (*a*) Shwachman, H.; Leubner, H., and Catzel, P.: Mucoviscidosis, Advances in Pediatrics **7**: 249, 1955. (*b*) di Sant'Agnese, P. A.: Fibrocystic Disease of the Pancreas with Normal or Partial Pancreatic Function: Current Views on Pathogenesis and Diagnosis, Pediatrics **15**: 683, 1955.

condition was under control. The age of onset of the pulmonary component varies greatly and ranges from a few days after birth to the age of several years. In the majority of cases the onset occurs between 6 months and 2 years of age. The general pattern of the respiratory disease is uniform,[9] except for the degree of severity, duration of single phases, and incidence of complications.

Acute respiratory infections initiate the cycle (table 2), causing increased mucus production. Failure to remove bronchial secretions, perhaps because of their abnormal physicochemical composition, leads to widespread, and at times severe, bronchial obstruction, and secondary infection follows, at times with great rapidity. Respiratory distress is present to a varying degree and may be severe, with cyanosis and air hunger. The patient is usually quite ill at this stage and presents the picture of severe generalized pulmonary infection. Spread of the bronchial infection to the blood stream or massive lobar atelectasis [9b] may occur at this stage and lead rapidly to death. More often, under the influence of antibiotic therapy, the bronchial infection is brought under tem-

TABLE 2.—*Sequence of Pulmonary Involvement in Fibrocystic Disease of the Pancreas*

Acute respiratory infection	
(Failure to remove bronchial secretions) *	
Bronchial obstruction	
Secondary bronchial infection	
(Irreversible damage to bronchi)	(No permanent damage to bronchi)
Severe progressive bronchopneumonia	Mild chronic pulmonary disease
Antibiotics unable to check disease	Antibiotics effective in prophylaxis
Pulmonary insufficiency	Improvement after 10 yr. of age
Death	(Chronic lung disease as adults)

* ( ) indicate steps that are probable but not proved.

porary control, but some degree of bronchial obstruction persists. The cycle is then repeated on the occasion of subsequent respiratory infections, thus explaining the characteristic course of the disease, punctuated as it is by relatively sudden attacks of markedly increased bronchial obstruction and secondary infection, any one of which may be fatal. Bronchial obstruction may thus be looked upon as the primary and cardinal manifestation of the pulmonary involvement of fibrocystic disease of the pancreas. Consequently, obstructive emphysema, with severely limited respiratory movements, poor alveolar aeration, anoxia, and carbon dioxide retention appears.

The physical examination and the roentgen picture are both characteristic if the chronic lung disease is marked. The chest is barrel-shaped and the note on percussion markedly tympanitic. On auscultation there are scattered rales that clear up temporarily after an episode of paroxysmal coughing. There is gradually increasing clubbing of fingers and toes. In roentgenograms the signs of marked generalized obstructive emphysema are present: increased anteroposterior diameter of the chest, flattened diaphragmatic leaves, and cardiothoracic index smaller than average. In addition, the signs of widespread, bilateral, chronic bronchopneumonia are seen; that is, a honeycomb appearance of the lungs or, at a more severe and advanced stage, a snowflake appearance similar to that of pulmonary tuberculosis. Peribronchial cuffing is generally marked even early in the disease. On nose and throat culture, and from the lungs at autopsy, a hemolytic Micrococcus (Staphylococcus) pyogenes var. aureus organism is usually recovered, unless therapy with wide-spectrum antibiotics has modified the flora.

Sudden death from asphyxia due to a large volume of thick, tenacious bronchial secretion suddenly mobilized by coughing has been observed several times. Three cases of spontaneous mediastinal and subcutaneous emphysema were seen in the present series. Lobar or multilobar atelectasis occurs in about 10% of patients. The sudden increase in intrapulmonary pressure characteristic of this disease may lead to rapid dilatation of the heart, with signs of circulatory embarrassment. If the patient survives, the heart rapidly returns to its normal size and function because of the intact myocardium in this young age group. Chronic cor pulmonale has been seen only in a small number of patients with long-standing, severe, progressive lung disease. The chronic bronchopneumonia in this condition may be initiated by measles or whooping cough. This is especially interesting in view of the time-honored observation that measles and whooping cough in some patients lead to chronic lung disease.

Liver.—For a long time it has been known [10] that occasionally infants and older children with fibrocystic disease of the pancreas were found at autopsy to have small areas of "focal biliary fibrosis" [6c] scattered throughout their livers. Also, occasionally patients at postmortem examination were found to have extensive cirrhotic changes in the liver. Only recently, however, has it been realized that the initial lesions occur commonly as an autopsy finding [6c] and may during life progress to widespread and clinically manifest cirrhosis of the liver with hepatosplenomegaly and portal hypertension.[5]

Focal biliary fibrosis is characterized by concretions of amorphous eosinophilic material plugging the bile ductules, biliary proliferation, inflammatory reaction, and absence of bile-staining. The nature of the concretions is not clear, but histologically and histochemically they resemble those found in the pancreas, which have been thought to be formed by inspissated secretions. On inspection of the liver at this stage a varying degree of pitting of the capsule is seen, corresponding to retraction of fibrous tissue in the cirrhotic foci. Twenty-five per cent of 116 autopsy cases at Babies Hospital [5] and a similar percentage in Bodian's series [6c] exhibited these changes at postmortem examination. The biliary fibrosis may be limited to a few areas and later become extensive, or it may be diffuse, but mild, from the beginning. Retraction of fibrous tissue may give rise to considerable lobulation of the surface of the liver. However, even when the lesions are extensive, their scattered character is such that, even though a significant amount of parenchyma is affected, there are no clinical or laboratory symptoms of involvement for a time.

9. di Sant'Agnese, P. A.: (*a*) The Pulmonary Manifestations of Fibrocystic Disease of the Pancreas, Dis. Chest **27**: 654, 1955; (*b*) Bronchial Obstruction with Lobar Atelectasis and Emphysema in Cystic Fibrosis of the Pancreas, Pediatrics **12**: 178, 1953.

10. Footnotes 2 and 6*b*.

In some patients the process, until then relatively localized, becomes generalized. Such a patient then goes on to a diffuse and severe hepatic cirrhosis that combines scarring and regenerative nodules with diffuse portal changes. On physical examination the liver is found to be moderately enlarged, hard, nontender, and frequently nodular. Chemical tests of liver function and serum bilirubin remain normal. After a varying length of time, a

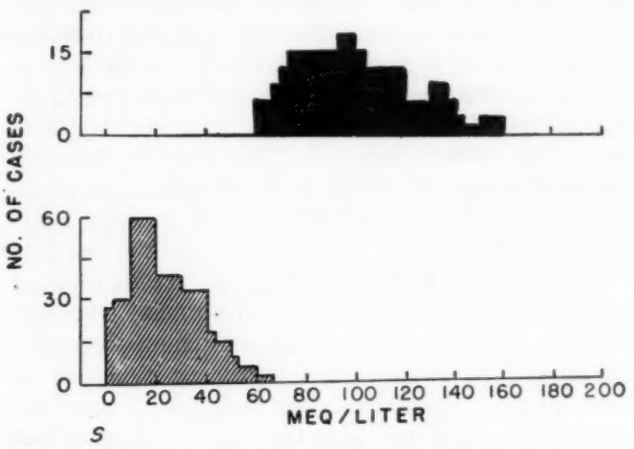

Fig. 1.—Sweat chloride values in 90 patients with fibrocystic disease of the pancreas and in 151 control subjects with normal health or miscellaneous diseases. Sweat is from midabdomen or scapular region. Black bar = patients with fibrocystic disease, striped bars = control subjects.

few months or a few years, the distortion and remodeling of the architecture of the parenchyma of the liver is such that portal hypertension eventually develops.[5] It is at this stage that the condition becomes clinically manifest, with the appearance of hepatosplenomegaly and later hypersplenia, gastrointestinal bleeding, or ascites, or a combination of the three. Liver function tests may become abnormal at this stage, but the serum bilirubin level is either normal or very slightly increased. Out of a total of 325 cases in the present series, in 7, or approximately 2%, the syndrome of portal hypertension was present. In some of these, the symptoms consequent on portal hypertension have dominated the clinical picture and determined the fate of the patient. While the total number is not large, it accounts for one-third of patients with this symptom complex in the pediatric age group.

Sweat Glands.—In 1953, in studies carried out at this hospital,[11] it was shown that patients with fibrocystic disease of the pancreas consistently exhibit a specific abnormality of sweat electrolytes. Sweat chloride and sodium are increased two to four times above the concentration found in normal individuals and in patients with a variety of other conditions not related to this disorder (fig. 1). (Sweat electrolyte values in patients with fibrocystic disease of the pancreas were: chlorine 60-160 mEq. per liter [mean 106 mEq. per liter] and sodium 80-190 mEq. per liter [mean 133 mEq. per liter]; sweat electrolyte values in control subjects were: chlorine 4-60 mEq. per liter [mean 32 mEq. per liter] and sodium 10-80 mEq. per liter [mean 59 mEq. per liter].) These conditions include acquired pancreatic deficiency (chronic pancreatitis, total pancreatectomy), chronic lung disease, cirrhosis of the liver, and many other diseases. In contrast to the marked discrepancy in electrolyte composition, the total volume of sweating per unit of time was not significantly different in patients with fibrocystic disease of the pancreas and controls.

During these investigations it was shown in metabolic studies that the increased electrolyte concentration of sweat in this disorder is not consequent on impaired kidney or adrenal function and that the sweat content of chloride and sodium is not greatly affected by administration of desoxycorticosterone, restriction of salt in the diet, or exposure of the patient to hot weather over a period of time. This is in marked contrast to the behavior of both normal individuals and patients with adrenal insufficiency. It was concluded therefore that the defect in patients with fibrocystic disease of the pancreas is in the sweat glands themselves. In addition, a survey of patients' relatives has shown in some,[11b] in the absence of pancreatic or pulmonary symptoms, the sweat electrolyte pattern characteristic of the disease. This sweat abnormality has also been found in the presence of chronic lung infection with normal pancreatic function (fig. 2) among the patients' relatives.

The findings just described gave rise to important pathogenic and diagnostic considerations, which will be discussed later. Furthermore, these findings have explained the unusual susceptibility to heat of patients with fibrocystic disease of the pancreas, which had been known for some time, and clarified the mechanism of death due to massive salt loss through the sweat of such patients in hot weather. These results were later confirmed by Shwachman and others.[8a]

Salivary Glands.—The secretory rate of the parotid glands is markedly increased above normal in patients with fibrocystic disease of the pancreas.[4b] This has been

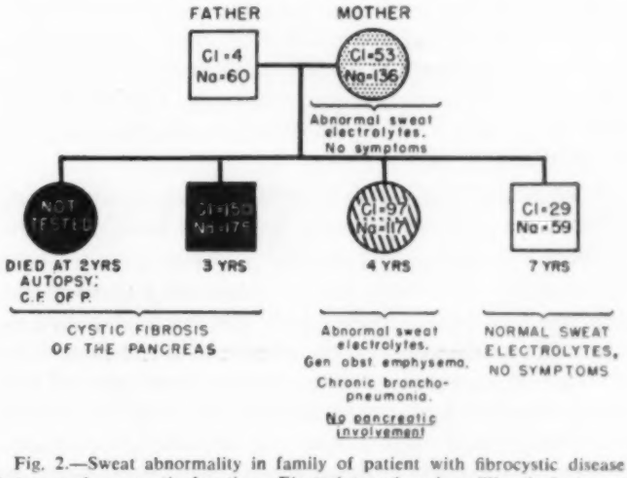

Fig. 2.—Sweat abnormality in family of patient with fibrocystic disease but normal pancreatic function. Electrolyte values in milliequivalents per liter. (Reprinted with permission from di Sant'Agnese.[8b])

thought in the past to be an indication of autonomic nervous system activity. The electrolyte concentration is also abnormally increased in mixed saliva in patients with fibrocystic disease of the pancreas as compared with controls.[4b] The overlap in values is considerable in the two groups; therefore, salivary electrolyte analyses are

11. (*a*) Footnote 4*a*. (*b*) di Sant'Agnese, P. A.; Darling, R. C.; Perera, G. A., and Shea, E.: Sweat Electrolyte Disturbances Associated with Childhood Pancreatic Disease, Am. J. Med. **15**: 777, 1953.

not useful in differential diagnosis. There is reason to believe, primarily on clinical evidence, that gastric secretions may be involved.[4b] What appears to be a minor amount of vomiting may lead to severe dehydration, hypochloremia, and metabolic alkalosis.

Viscosity, Mucopolysaccharide Structure, and Electrolyte Composition of Duodenal Contents.—Physicochemical changes in mucous secretions have been suggested to explain some of the clinical and pathological changes seen in fibrocystic disease.[12] Studies are being conducted in this hospital [13] on the chemical structure of mucopolysaccharides in body fluids of patients with the disease as compared with control subjects. Results indicate the presence in duodenal fluid of a mucoid consisting of a carbohydrate and protein residue. The carbohydrate moiety contains galactose, hexosamine, and fucose. The proportions of these three sugars are very similar to those found in other forms of mucus. In addition, however, a hexosan is found in the duodenal fluid that does not seem to be identical with glycogen. So far, no significant difference in the composition of this mucoid fraction has been found in normal individuals and patients with cystic fibrosis of the pancreas. Patients with this condition, however, contain, in addition, in their duodenal juice still another glycoprotein, which differs in its physical characteristics and chemical composition from the previously described mucoid. This fraction is not found in the duodenal contents of normal control subjects.

The duodenal contents are frequently found to be abnormally viscous,[8a] and this may be the first manifestation of the disease, preceding at times pancreatic deficiency. Increased viscosity is therefore an important finding, but its significance is obscure, as it seems to vary independently from pancreatic function.[8b] There also appears to be no correlation between structure of mucopolysaccharides and abnormal viscosity.[13] Electrolytes in duodenal contents of patients with fibrocystic disease, with and without pancreatic deficiency, and in control individuals with a variety of other conditions appear to be identical.[4b]

Meconium Ileus.—About 10% of patients with fibrocystic disease of the pancreas present at birth a picture of intestinal obstruction due to inspissated meconium, the so-called meconium ileus.[14] Deficiency of exocrine pancreatic secretions before birth has been advanced as a possible explanation for the abnormal meconium. The obstruction is usually located in the distal part of the small intestine, and, proximal to it, the ileum is dilated and filled with a large amount of tenacious, viscid meconium. This leads at times to a twisting upon itself of the dilated segment, resembling a volvulus. Intrauterine perforation of the intestine due to the obstruction may lead to widespread sterile peritonitis, so-called meconium peritonitis. It is important to realize that the same picture of acute antenatal peritonitis may follow other types of intrauterine obstruction (e. g., intestinal atresia), although meconium ileus, in my experience, has been its commonest cause. Out of the 325 patients, 40 have had meconium ileus and 6 of these, meconium peritonitis in addition.

12. Footnote 6*b* and *c*.

13. Dische, Z., and di Sant'Agnese, P. A.: Composition of Mucopolysaccharides of Intestinal Juice in Patients with Fibrocystic Disease of the Pancreas and Controls, to be published.

14. Footnotes 2, 6*c*, 7*b*, and 8*a*. Hiatt, R. B., and Wilson, P. E.: Celiac Syndrome: VII. Therapy of Meconium Ileus: Report of 8 Cases with Review of the Literature, Surg. Gynec. & Obst. 87: 317, 1948.

Diagnosis

The clinical manifestations of fibrocystic disease of the pancreas depend on whether the pancreatic, pulmonary, or hepatic involvement, or a varying combination of the three, predominates (table 1). In the average case the combination of the symptoms of pancreatic deficiency and of chronic respiratory disease leads one to suspect the correct diagnosis. Until recently, definitive clinical diagnosis has rested on the demonstration of absence of pancreatic enzymes in duodenal contents. However, while adequate in a majority of cases, this test does not help in those patients in whom pancreatic function is still partially preserved or even normal. Duodenal drainage, furthermore, is a time-consuming procedure, and an analysis of the fluids for enzymes is difficult for many hospital laboratories. The search for a simplified diagnostic method has led to the elaboration of various tests, all of them, however, dependent on the presence of pancreatic deficiency. The finding of an abnormal electrolyte concentration in sweat [11] has furnished a valuable diagnostic tool in the investigation of fibrocystic disease and one that is not dependent on the function of the pancreas. The introduction by Shwachman [8a] of a plastic bag to make patients sweat, instead of the constant temperature room, further simplifies the procedure and brings it within reach of most hospital laboratories. The analysis of sweat for chloride and sodium is then carried out as originally described by me.

Four diagnostic criteria should be followed in arriving at a diagnosis of fibrocystic disease of the pancreas (table 1): pancreatic deficiency, pulmonary pathology, abnormal sweat, and family history. 1. There is complete absence of pancreatic exocrine function in 90% of patients. Duodenal assay reveals absence of pancreatic ferments. As a simple screening test microscopic examination of the stools for the presence of excess of fat has proved satisfactory if pancreatic deficiency is present. Less reliable in my experience has been the absence of tryptic activity in the stools of such patients, demonstrated by inability of appropriate dilutions of fecal material to digest the gelatin on photographic film. 2. Pulmonary pathology, with obstructive emphysema, chronic bronchopneumonia, or both, is found in varying degrees of severity in virtually all patients at some time in the course of the disease [9] and, while not pathognomonic, points strongly towards the diagnosis. 3. Abnormal sweat with characteristically increased concentration of sweat chloride and sodium is present in 99% of patients. 4. The occurrence of the disease in siblings is of diagnostic assistance; its absence, however, does not rule out the condition in the patient. In addition, the combination of cirrhosis of the liver with portal hypertension and chronic pulmonary disease with generalized obstructive emphysema is very suggestive of fibrocystic disease even in the absence of pancreatic involvement. An abnormal "sweat test" will support the diagnosis.

Prognosis

The fate of patients with fibrocystic disease of the pancreas is usually determined by the course of the pulmonary disease.[15] Pancreatic involvement affects the child's state of nutrition, his growth, and his development but per se plays a relatively small role in survival. It must be kept in mind that the pulmonary component of fibrocystic disease of the pancreas is an intrabronchial disease, which does not primarily affect the walls of the respiratory passages. Permanent damage to the bronchi is the result of severe and prolonged infection secondary to bronchial obstruction (table 2). If irreversible damage is done to the bronchial wall, the patient goes on to severe progressive bronchopneumonia, unresponsive to antibiotic therapy. The distressing picture of pulmonary insufficiency develops and leads to death in two or three years. At any time, however, events may take a precipitous turn, leading rapidly to fatal termination. If secondary infection does not cause permanent damage to the bronchi, the resulting mild chronic lung disease can be kept in check by the prophylactic administration of broad-spectrum antibiotics. When patients reach late childhood without permanent pulmonary injury, they improve and the degree of clearing in the roentgen picture is surprising. Pulmonary function at this time may be virtually normal. What the future holds for such patients is hard to say, but one suspects that many will show chronic pulmonary disease as adults.

Although less important to the patient's ultimate outlook, attention should be paid to the effects of pancreatic insufficiency. Maintenance of good nutrition, improvement in the character of the stools, and avoidance of vitamin deficiencies can usually be accomplished by a dietary regimen.[16] Beneficial results as to growth and development are less consistent but frequently good. Symptoms resulting from deficiency of pancreatic enzymes vary considerably, even among patients with complete absence of pancreatic function. With advancing age, as a general rule, there is less need for severe dietary restrictions; but, the changes in the pancreas are not reversible, and dietary restriction, even though relaxed, will have to be continued indefinitely.

The life of a patient with fibrocystic disease of the pancreas is fraught with dangers. In early infancy intestinal obstruction due to meconium ileus may occur. Hepatic lesions may occasionally progress to manifest cirrhosis of the liver with portal hypertension and the dangers of severe and uncontrollable gastrointestinal hemorrhage. Salt depletion through the sweat may lead to death in hot weather. Although fibrocystic disease of the pancreas, therefore, is a serious condition and the prognosis at best guarded, the outlook is by no means hopeless. Of 325 patients seen in 15 years, 145 are dead and 168 are living; the other 12 cannot be traced. Twenty-four are above the age of 10 years; the oldest one followed in this hospital is 19 years old and doing well.

Treatment

Treatment of patients with fibrocystic disease of the pancreas is directed primarily toward correcting the effects of pancreatic deficiency (when present) by means of dietary measures and controlling the respiratory disease by administration of antibiotic agents. The principles of dietary therapy are outlined in table 3. A more detailed discussion can be found in a report by Andersen.[16] Antibiotic treatment (table 3) is required by all patients who have respiratory involvement.[17] As the basic infection is due to a hemolytic M. pyogenes var. aureus organism, penicillin, by intramuscular injection and by inhalation, is given. A wide-spectrum antibiotic is added by mouth. If the nose and throat cultures reveal gram-negative bacteria, streptomycin, both by intramuscular injection and by inhalation, is added. Intensive treatment is usually given for a period of not less than 7 and not more than 15 days. Dosages are detailed in table 3. Recently, 40-50 mg. of erythromycin per kilogram of body weight every 24 hours, with 0.1 gm. of sulfisoxazole (Gantrisin) per kilogram every 24 hours, has been successful at times. If respiratory involvement persists after treatment, as it usually does, continued administration of one of the broad-spectrum antibiotics in prophylactic doses is advisable. This may have to be continued for months or years until all clinical and laboratory signs of pulmonary infection disappear. Emergence of resistance to antibiotic agents has caused increasing concern; however, despite this possibility, continued administration of these drugs is imperative. Many of the strains of a hemolytic M. pyogenes var. aureus organism isolated recently from the nasopharynx of these patients have been found resistant to most antibiotics, with the exception of chloramphenicol (Chloromycetin).

Therapeutic bronchoscopy is usually contraindicated because of the difficulty of examination in children, because of the adverse reactions that it frequently gives

TABLE 3.—*Dietary, Antibiotic, and Other Therapies in Treatment of Fibrocystic Disease of Pancreas*

Dietary
Diet
High-caloric (150-200 calories/kg of body weight in infants)
High-protein (2-6 gm./kg.)
High-simple-sugar (glucose, cane sugar, banana, etc.)
Low-fat, moderate starch
Liposoluble vitamins (2,000 units vitamin D/day and 10,000 units vitamin A/day)
Pancreatic extracts—with each meal
Additional oral intake of salt—liberal salting of foods and 2 gm./day additional salt during hot weather
Antibiotic *
Therapeutic course (7-15 days)
Intramuscular (procaine penicillin, 800,000 units/day; streptomycin, 1 gm./24 hr., or 40 mg./kg.)
Inhalation (penicillin, 100,000 units 5 times a day; streptomycin, 200 mg. 5 times a day †)
Oral (broad-spectrum antibiotic—one of the tetracyclines or chloramphenicol—50 mg./kg./24 hr.)
Prophylactic administration (as long as there is roentgen evidence of respiratory involvement)
Oral (broad-spectrum antibiotic—one of the tetracyclines or chloramphenicol—10-20 mg./kg./24 hr. for maximum of 500 mg./day)
Other
Therapeutic bronchoscopy—usually contraindicated
Lung surgery—usually not indicated because of generalized nature of lung involvement
Surgery—required by patients with meconium ileus and cirrhosis of liver with portal hypertension

* All dosages in treatment of respiratory infection for children.
† Penicillin and streptomycin to be added together to 2 cc. of sodium chloride and nebulized (Vaponefrin nebulizer) with oxygen or compressed air flowing at 5 to 6 liters/min.

15. Footnotes 7*b* and 9.
16. Andersen, D. H.: Celiac Syndrome: III. Dietary Therapy for Congenital Pancreatic Deficiency, Am. J. Dis. Child. **70**: 100 (Aug.) 1945.
17. Footnotes 7*b*, 8*a*, and 9*a*.

rise to, and because of the lack of improvement after the procedure. Lobectomy or partial pneumonectomy for bronchiectasis is not indicated in most instances because of the generalized nature of the pulmonary involvement. Lobectomy for atelectasis should be considered only if lobar collapse has persisted unaltered for more than one year. Spontaneous expansion of a collapsed lobe may appear even after months.[9b] Furthermore, lobectomy performed for this purpose has generally failed to modify the progressively downhill course of the disease. Postural drainage has been of help in some patients.

In view of the frequency with which measles is followed by serious complications in patients with fibrocystic disease of the pancreas, every effort should be made to prevent or modify this disease by the administration of gamma globulin, if exposure is known. If the patient has measles, prophylactic antibiotic treatment is indicated. Immunity against whooping cough should be kept up by regular booster injections of vaccine. Administration of digitalis for brief periods may help the patient overcome transient circulatory embarrassment secondary to an exacerbation of the chronic pulmonary infection.

Meconium ileus in the newborn infant must be relieved surgically. If operation is successful, the subsequent management follows that of other patients with fibrocystic disease of the pancreas. In some patients with cirrhosis of the liver, surgical shunting procedures may be necessary in an attempt to relieve excessive portal pressure, thus decreasing the dangers of uncontrollable gastrointestinal hemorrhage.[5]

Acute salt loss through the sweat should be suspected when patients with fibrocystic disease of the pancreas are admitted to hospital with symptoms of vomiting and dehydration [4a] during a period of hot weather. Thirst is an unreliable symptom. Hyperpyrexia, cardiovascular collapse, and, at times, coma represent a further step in salt depletion and bring about an acute medical emergency. The patient may be in imminent danger of death unless prompt and vigorous measures are undertaken to restore the depleted water and electrolyte stores. Sodium chloride intravenously is therefore urgently needed.

Comment

Our conception of the nature of fibrocystic disease of the pancreas has changed in the last few years. The theory was first advanced of the existence in this disease of an abnormality of mucous secretion,[6b] which would account for many of its symptoms and pathological changes. This view for a time drew considerable support.[18] However, the demonstration of the consistent occurrence of a specific abnormality of sweat [11] has greatly broadened our concept. The evidence that yet another glandular system (and one that is not mucus-producing) is consistently involved gives confirmation that fibrocystic disease of the pancreas is a generalized disorder in which many and perhaps all exocrine glands, mucus-producing and others, are affected. Furthermore, the demonstration of the existence of the characteristic sweat electrolyte pattern in relatives of known patients with normal pancreatic function and with or without pulmonary involvement has led to the belief that incomplete and milder forms of the disease exist. The findings suggest further that involvement of these organs is independent of each other. Varying degrees of involvement of the pancreatic, pulmonary, and hepatic areas give rise to different clinical pictures. It is possible of course that in all instances all organs are affected but to an extent that is not sufficient to interfere with function and give rise to clinical manifestations. Symptoms may appear later [8b] or remain in abeyance indefinitely. The basic nature of this widespread disorder is not known as yet, but it appears to be genetically transmitted. A recessive mechanism has been postulated.[19]

The name fibrocystic disease of the pancreas is erroneous, because this generalized condition is not a disease of the pancreas but one in which this organ is usually, but not necessarily, involved. By the same token, the name "mucoviscidosis" [8a] is improper, because it leads to the belief that only the mucus-secreting structures are affected. With the demonstration of the consistent involvement of sweat and parotid glands,[4] both of them non-mucus-producing, this is no longer a justified belief. Use of these terms tends to prolong an erroneous concept and introduces another improper term to further confuse an already unclear field. A name such as "generalized exocrinopathy" would certainly be more justified in the present state of our knowledge. However, a plea is made for retention of the term fibrocystic disease of the pancreas, a "most unsatisfactory name, but one which will have to stand until a better one is proposed" [20]—perhaps until the etiology of the disease is clarified.

Summary

Fibrocystic disease of the pancreas is a hereditary disease of children in which the exocrine glands are affected. It occurs in Caucasians but is rare in Negroes. In the past 15 years, 325 patients have been observed and followed at Babies Hospital. Attention was first focused on the pancreas (as the name implies), but it was soon realized that pulmonary involvement, frequently severe, was present in almost all cases. It was recently shown that sweat and salivary glands, and less often the liver, are consistently affected in this disorder. In patients with this disease the sodium chloride content of sweat is increased two to four times above the concentration found in normal individuals and in a variety of other conditions. Massive salt loss through the sweat in hot weather may cause the death of these patients. This finding is also of great diagnostic assistance. While fibrocystic disease of the pancreas has been difficult to diagnose in the past, the simplicity of the "sweat test" brings it within reach of most hospital laboratories. The fate of patients with fibrocystic disease of the pancreas is usually determined by the severity of the pulmonary involvement. The outlook depends on success in controlling the chronic respiratory disease with antibiotic agents.

Our conception of the basic nature of fibrocystic disease of the pancreas has greatly changed in the last few years. At first it was thought to be limited to an abnormality of mucous secretion; however, the finding of the

18. Footnotes 6c and 8a.

19. Footnotes 6c, 7b, and 8a. Andersen, D. H., and Hodges, R. G.: Celiac Syndrome: V. Genetics of Cystic Fibrosis of the Pancreas with a Consideration of Etiology, Am. J. Dis. Child. 72: 62 (July) 1946.

20. Gellis, S.: Editor's note, in Yearbook of Pediatrics, Chicago, Year Book Publishers, Inc., 1954, p. 230.

consistent occurrence of an electrolyte abnormality of sweat has greatly broadened the concept by showing that many and perhaps all exocrine glands, mucus-producing and others, are affected. Furthermore, the occurrence of the characteristic sweat electrolyte pattern in relatives of known patients, with or without pulmonary involvement but with normal pancreatic function, has led to the belief that milder and incomplete forms of the disease exist. This generalized glandular disorder accounts for virtually all cases of pancreatic deficiency in the pediatric age group, for a majority of those with chronic (nontuberculous) lung disease, and for a third of children with cirrhosis of the liver and portal hypertension. It deserves, therefore, greater recognition by the medical profession than has been accorded it in the past.

622 W. 168 St. (32).

ESTIMATION OF OPERATIVE RISK IN 1955

Carl A. Moyer, M.D.
and
J. Albert Key, M.D., St. Louis

The appraisal of the operative risk to be assumed by an individual is a sketchy, intuitive evaluation of the probability of dying during an operation and convalescence. The word probability bears statistical implications and infers the formulation of a judicious estimate of the magnitudes of the factors jeopardizing the person's life while the physiological deformations attendant upon the operation and the individual's illness are operative.

A truly statistical approach to the assessment of the probability of operative death is impossible because there are insufficient data pertinent to the influences of age, nutrition, length of illness, and cardiac, pulmonary, renal, or other disease upon a man's capacity to live during and after a particular operation. All that is possible today is the making of a gross estimate of risk based upon the recollection of the outcome of similar operations, performed by oneself and others, upon individuals of similar age and biological decrepitude. Obviously, in estimating operative risk on this basis, biased selection is especially prone to influence one's judgment because the unrecorded experiences of the surgeon and internist are the important bases for the estimate of probability. Consequently, such an important resolve as the assessment of operative risk now is based in large part upon hazardous grounds—yet it must be done this way until more precise methods are developed.

Generally the magnitude of operative risk is overestimated, and, by virtue thereof, the individual suffering from a surgically remediable illness may be denied the opportunity of having his trouble removed. The operative risk attending practically all operations is significantly less today than it was two and three decades ago. Figure 1 and table 1 demonstrate the remarkable reductions in operative risk that have transpired during three decades. Obviously the surgeon or internist old enough to have been a house-officer or medical student 20 or more years ago will have had an impressive personal experience with the great magnitude of the dangers attending many operations and consequently now will overweight the risk of these operations unconsciously because the estimation of this risk is dependent upon his memory of past experience.

Read before the Section on Surgery, General and Abdominal, at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 7, 1955.

• *Choledochostomy in the period from 1916 to 1938 had a mortality risk of 16%. The corresponding figure for the period 1948 to 1952 was 2%. Similar declines in mortality risks are found for eight other types of surgical operation.*

Earlier figures for operative mortality showed a significant difference between old and young patients. The difference has become insignificant in recent figures because the prognosis for older patients is now so much better.

The degree to which a patient's strength has been undermined by a long period of preoperative stress is difficult to evaluate. It is one important factor in determining operative risk; another factor is the efficiency of the surgical team. The importance of other factors has been so greatly reduced that there is need for reappraisal of surgical mortality rates.

Variance in Effect of Aging on Operative Risk

The aged and persons suffering from cardiac and pulmonary diseases are especially likely to be denied the surgical remedy of cholecystic disease, hernias, stasis ulcers, hemorrhoids, nodular goiters, painful skeletal deformities, and neoplastic disease because of the intuitive conviction, held by most of us, that aging reduces one's capacity to recover from any operation. Upon comparing the experiences of physicians recorded during the last decade with those recorded 20 years earlier, one is struck with the falsity of the general adage—the older the person, the greater is the operative risk. Tables 2 and 3 and figures 2 and 3 illustrate the variance in the effect of aging upon operative risk. The operative death rates for the operations listed in table 2 and illustrated graphically in figure 2 are higher among the aged than among the young; while, for those operations shown in table 3 and figure 3, the operative death rates are the same among the old and the young. The published observations of Cole and the Drs. Mithoefer were the first to show that the effects of aging upon operative risk varied widely and that they were nonexistent for a number of major operations.

A cursory search for the factors that are responsible for the lack of influence of aging upon the operative risk obtaining with some operations and the presence of in-

fluence with others lead to the inference that the magnitude of the operation is not as important a determinant of operative risk among the aged as is the duration of the period of physiological upset attending it.

Radical operations upon the mouth and neck for cancer, with their various combinations of mandibular, lingual, and cervical tissue resections, are prone to be attended by a rather prolonged period of physiological deformation that is incident to oral sepsis, dislocation of deglutition, disturbances in breathing, and alteration of the intracranial vascular bed especially with bilateral internal resections of the jugular vein. The combined abdominal-perineal resection of the rectum and sigmoid colon is rather often followed by a prolonged illness accountable to sepsis, vesical obstruction, or postoperative intestinal obstruction. Physiological recovery from pneumonectomy and closure of perforated gastric and duodenal ulcers also tends to be long. With these operations the operative risk is significantly higher among the aged than among the young. In contrast the periods of physiological deformation after radical mastectomy, thyroidectomy, cholecystectomy, herniorrhaphy, and partial gastrectomy for duodenal ulcer are relatively brief and the operative risks for the aged and the young are similar. The differences that exist between them are insignificant.

Certainly, a radical mastectomy is a more formidable procedure from the anatomic, temporal, and blood-loss standpoints than is the closure of a perforated ulcer—so too is cholecystectomy a longer and more difficult procedure than closure of a perforated ulcer. However, the operative risks are remarkably low for cholecystectomy and radical mastectomy and are similar for both young and old persons, while for closure of a perforated ulcer they are relatively high and the risk for the aged is much higher than that applicable to the younger age group. These relationships support the statement previously made: "The magnitude of the operation is not as important a determinant of operative risk among the aged as is the duration of the period of physiological upset attending it."

Undoubtedly, the betterment of the treatment of sepsis has contributed to the reduction of operative risk among the aged and the young during the past 15 years. Cholecystectomy and appendectomy were long associated with a rather high incidence of postoperative infections, and these procedures in the aged were attended by disproportionately high operative death rates 10 and 20 years ago. This is shown in figure 4. Coincident with the introduction of therapy with antibiotics significant reductions occurred in the operative mortalities attending cholecystectomy and appendectomy. The performance

TABLE 1.—*Change in Operative Risk Between 1916-1938 and 1948-1953* *

Operation	1916-1938 Time Period	1916-1938 Operative Mortality, %	1948-1953 Time Period	1948-1953 Operative Mortality, %
Choledochostomy	1916-1938	16	1948-1952	2
Thyroidectomy for toxic goiter	1920	5-8	1953	1
Closure of perforated peptic ulcer	1935	41	1949	7
Correction obstructions of small intestine	1928	37	1950-1953	8
Esophagectomy for cancer	1933	55	1952	16
Partial gastric resection for duodenal ulcer	1936-1945	4	1952	2
Surgical therapy of colonic wounds	1941	62	1953	14
Surgical therapy of hepatic wounds	1934	62	1953	10
Radical mastectomy	1925	1	1952	0.2

* The combined unit surgical mortality rate of the above procedures between 1916-1938 was 34.1%, while it was 7.6% between 1948 and 1953. The 1948-1953 rate was but 22% of the 1916-1948 rate.

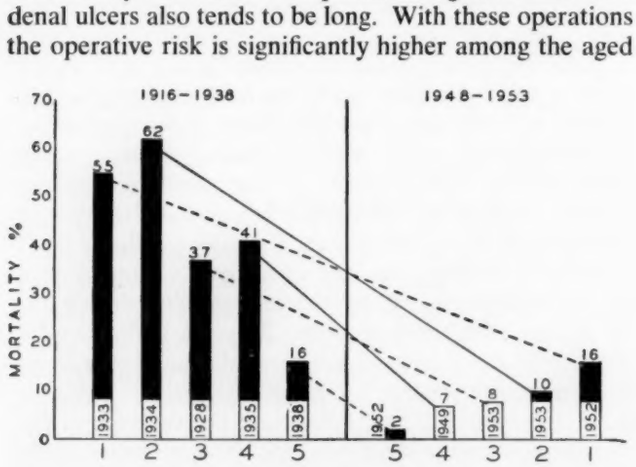

Fig. 1.—Reduction in operative risk during three decades. 1 indicates esophagectomy for cancer; 2, surgical therapy, hepatic wounds; 3, correction, obstruction small intestine; 4, closure, perforated peptic ulcer; 5, choledochostomy.

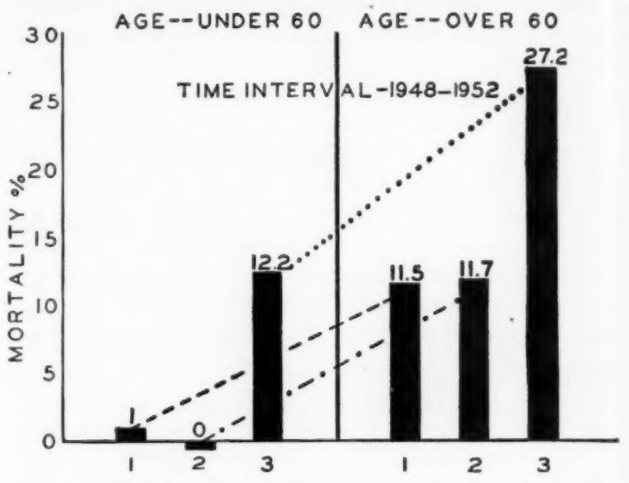

Fig. 2.—Effect of aging on operative risk. 1 indicates "radical" surgery for cancer of mouth and neck; 2, radical resection of rectum for cancer; 3, pneumonectomy.

TABLE 2.—*Operative Death Rates in Group of Patients Showing Higher Death Rates Among the Aged than Among the Young*

Operation	Age, Yr.	Mortality, %	No. in Series	Time Period	P *
Closure of perforated peptic ulcer	20-39	5	41	1935-1941	0.01
	40-59	15.6	64		
	60-79	40.0	28		
Radical surgery for cancer of mouth and neck	Under 60	1.0	105	1948-1952	0.001
	Over 60	11.5	121		
Cholecystectomy with and without choledochostomy †	Under 70	1.18	513	1944-1951	0.01
	Over 70	5.7	70		
Radical resection of rectum for cancer	Under 60	0.0	53	1948-1952	0.01
	Over 60	11.7	62		
Gastrectomy for duodenal ulcer ‡	Under 40	1.3	77	1940-1950	0.05
	Over 40	7.9	240		
Pneumonectomy	Under 60	12.2	49	1948-1952	0.01
	Over 60	27.2	18		

* Probability that death rates for the aged and the young will be the same.

† Between 1948 and 1952, Cole found no significant difference between individuals less than and over 60 years (see table 3 and fig. 3).

‡ At variance with Cole's later finding (see table 3).

of cholecystectomy upon 100 persons under 60 years of age today is attended by 3 fewer postoperative deaths than it was 15 years ago, while the performance of cholecystectomy upon 100 persons over 60 years of age today is attended by 11 fewer deaths than it was 15 years ago. To be sure, antibiotics have not effected all of this alone. Other factors, such as greater skill in administering anesthetics, fluids, and blood, have been acquired concomitantly.

Need for Reappraisal of Mortality Rates

Such demonstrations of what has been accomplished in reducing the postoperative mortality among the aged during the past two decades should convince one that aging of itself is not an insuperable barrier to the attainment of humanely and socially acceptable operative risks. In addition they should make us conscious of the great need for assiduous studies of the mortality rates attending the laissez-faire therapeutics for the aged suffering such entities as relatively symptomless cholelithiasis, inguinal, incisional, and diaphragmatic hernias, chronic localized suppurative diseases of lung, occlusive disease of major arteries, extensive colonic diverticulosis with massive hemorrhage or diverticulitis without obstruction, so-called nontoxic nodular goiters, polypoid lesions of the stomach, and painful degenerative lesions of the hip and knee. Without the reappraisal of the consequences of the laissez-faire management of entities such as these, we shall be unable to weigh the relative merits of procrastination and a corrective elective operation for patients of advanced years having specific physical troubles. It is likely that after the performance of such studies advanced old age will no longer constitute an excuse for such statements as these: "I would advise an operation would he be but 10 years younger. He is too old to take an anesthetic. He's so old that I am afraid his heart won't stand the operation."

TABLE 3.—*Operative Death Rates in Group of Patients Showing Same Rates Among the Aged as Among the Young*

Operation	Age, Yr.	Mortality, %	No. In Series	Time Period	P *
Esophagectomy for cancer	Under 60	29.4	17	1948-1952	0.4
	Over 60	41.9	31		
Colectomy	Under 60	4.6	43	1948-1952	0.6
	Over 60	7.7	26		
Radical mastectomy	Under 60	0	122	1948-1952	...
	Over 60	1.8	54		
Cholecystectomy	Under 60	0	169	1948-1952	>0.1
	Over 60	1.8	54		
Thyroidectomy	Under 60	0	287	1948-1952	...
	Over 60	0	44		
Herniorrhaphy	Under 60	0.3	313	1948-1952	0.3
	Over 60	1.5	68		
Partial gastrectomy for cancer	Under 60	5.8	34	1948-1952	0.5
	Over 60	2.8	36		
	Under 40	17.7	17	1940-1950	0.7
	Over 40	13.2	59		
Partial gastrectomy for peptic ulcer	Under 60	1.5	67	1948-1952	0.6
	Over 60	0.0	24		

* Probability that death rates for the aged and the young will be the same.

Much emphasis has been placed upon the potentiation of operative risk by pulmonary-cardiac diseases and the more especially among the aged. However, as more surgical experience is gained with persons having pulmonary-cardiac diseases, these diseases have become less important as determinants of operative risk. In fact, excepting the existence of angina pectoris, malignant hypertension, repeated myocardial infarction, and uncontrolled cardiac failure, the pulmonary-cardiac status of the individual affects the operative mortality rate very little.

The Drs. Mithoefer determined the operative mortality rates in two groups of aged persons. One group consisted of persons having no signs of significant cardiac or pulmonary abnormality preoperatively; the other, of persons having readily detectable signs of cardiac or pulmonary disease. The operative mortality rates were comparable. This observation led them to conclude that cardiopulmonary disease had no apparent influence upon the surgical mortality rate among the aged excepting when associated with angina pectoris. As stated before, malignant hypertension, uncontrolled cardiac failure, and repeated myocardial infarction increase operative risk regardless of the age of the person.

Fig. 3.—Effect of aging on operative risk; time interval: 1948-1952. 1 indicates cholecystectomy; 2, thyroidectomy; 3, gastric resection for cancer; 4, radical mastectomy.

Anesthesia has long been incriminated as an important factor in operative risk. In reality it is comparatively unimportant. Only in the case of operations of inherently little risk such as herniorrhaphy, appendectomy, and thyroidectomy will anesthesia of itself contribute significantly to the total operative mortality. The studies of Beecher and Todd substantiate the above statements. Among 8,137 postoperative deaths, anesthesia was designated as a primary and contributory factor in only 384. In the same series the patient's disease was judged to have been the cause of death 6,325 times and surgical error 1,428 times. In this series of cases 60% of the anesthesias were performed by nurse-anesthetists and residents. Obviously, although anesthesia deaths constitute a significant number, they are comparatively few when compared to those attributable to surgical error.

Operation	Age	Mortality Per Cent		
		1941		1951
Cholecystectomy	10 - 60	4.0		1.1
	61 and older	16.6		5.7
	Difference	12.6		4.6
		1928	1927-1931	1940-1949 5th decade only
Appendectomy for simple and complicated appendicitis	0 - 60	0.4	4.1	0.7 (274)
	61 and older	54	24.0	4.5 (88)
	Difference	53.6 (Fitch)	19.9 (Boland)	3.8 (Wolff)

Fig. 4.—Changing relationship of operative risk to age.

In other words, the surgeon should look upon himself as a far more important operative risk factor than anesthesia and the anesthetist and recognize that for some surgically remediable diseases the surgeon, or he who calls himself one, may be the major factor in the assessment of the operative risk today.

4580 Scott Ave. (10) (Dr. Moyer).

PREEMPLOYMENT EXAMINATIONS OF THE LOW BACK

Rex L. Diveley, M.D.
and
Rial R. Oglevie, M.D., Kansas City, Mo.

• *Examination of 6,523 prospective employees revealed congenital anomalies of the lumbosacral region in 41% and other abnormalities in 19%. In a former series of 3,587 employees who sought treatment for low back pain or disability, the group having congenital defects was likewise the largest, with 31%. The three most frequent congenital defects were malformed lumbosacral articulating facets, spina bifida occulta of the first sacral segment, and supernumerary lumbar vertebrae.*

Most applicants were not aware of the weakness. Preemployment examination, followed either by rejection or by assignment to limited duty when indicated, costs little as compared to the dollars and man-days saved by reducing the incidence of reported low back injuries.

Some five years ago we instituted a study to ascertain the end-results of treatment on patients complaining of low back pain and disability. This study covered a period of 20 years and an analysis of 3,587 treated cases. The results of our study were reported to the American Academy of Orthopaedic Surgeons at their meeting in Los Angeles in January of 1955. Several questions that resulted from this analysis are still unanswered, the principal one being "what number of these low back injuries could have been prevented by selective employment or activity?" To answer this query, and stimulated by several excellent reports on this subject, we added to our study the gathering of statistics on preemployment examinations of the back.

While there have been some excellent studies made on this subject and some interesting papers published, the conclusions are still not final. It would appear that, if the conclusions reached are to be of value and are to act as a guide for selective employment, more concentrated and supervised effort must be made to collect statistics on preemployment examinations. There can be little question as to the importance of this subject, since most industrial and orthopedic surgeons, as well as insurance carriers, admit that low back injuries and disabilities result in the loss of more money and man-days than any other compensable condition. In the current study the cost to the employer of back disabilities over an average year accounted for approximately 50% of the entire cost of all types of injuries and disabilities.

This study of preemployment examinations of the low back was begun by one of us (R. R. O.) in 1941 at a coffee-processing plant employing an average of 380 people. The reduction of the number of back injuries and the man-days lost from those injuries was so impressive that the same program was expanded to cover the employees of a large electrical plant working on war production and employing approximately 4,700 people. At the coffee company the principal hazard was the handling of 200-lb. bags of coffee, while there were many types of heavy lifting in the war plant, but with excellent supervision. The preemployment examinations in both plants included a thorough history with special emphasis on previous back injuries, a complete general examination, x-ray examination of the chest, and a careful physical and x-ray examination of the back. The roentgen examination of the spine included an anterior-posterior and lateral projection of the lower thoracic, lumbar, and sacral spinal segments, and, in questionable cases, oblique views of the lumbosacral area. The material for this paper consists of the results of the examination of 6,523 prospective employees, 4,902 of them from the war plant analyzed over a period of 3½ years and 1,621 of them from the coffee company analyzed over a period of 13 years. Of the employees examined, 86.3% were male and 13.7% were female. The age range was from 17 to 53 years, the average being 30.7 years.

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Findings

Our first problem was to determine which of the applicants had physical signs of low back disability or x-ray findings of structural weakness of the lower spine. Our findings in the x-ray studies are outlined in table 1. In explanation of the classifications used in this table, attention must be called to the fact that a clean-cut determination of the findings in each case was difficult, as in many cases there were overlapping structural weaknesses or pathology. The category into which each case was grouped was determined by the most outstanding finding in that case.

The congenital defects, listed in the order of their occurrence, were as follows: malformed lumbosacral articulating facets, spina bifida occulta of the first sacral segment, supernumerary lumbar vertebrae, sacralized last lumbar vertebra, cleft or failure of fusion of the last lumbar vertebra, spondylolisthesis, and four lumbar vertebrae.

By wear-and-tear changes of the lumbosacral joint is meant the general settling and narrowing of the space between the last lumbar vertebra and the first sacral segment, with resulting arthritic changes. Postural scoliosis denotes a correctable curve of the spine generally due to a tilt of the pelvis as the result of a short leg. Advanced arthritis indicates those cases in which atrophic or hypertrophic changes were noted in two or more vertebral segments. By structural scoliosis is meant long-standing curvature of the spine with rotation, with the spine fixed in the deformed position and difficult to correct. Increased lumbar lordosis denotes advanced anterior-posterior spinal curvature, with dorsal kyphosis and a resulting hollow back or increased lumbosacral inclination. Very few applicants gave a history of previ-

ous spinal injury or low back disability, yet in some cases a compression fracture was found or opaque material was evident in the neural canal. Further questioning then refreshed the applicant's memory of a previous accident and/or a low back examination.

It is interesting to compare the results of the x-ray studies in the present preemployment examinations with the findings in our reported series of 3,587 patients who sought treatment for low back pain or disability (table 2). On the basis of the preemployment examinations, employment was refused to 3.6% of all applicants, while 12.5% were assigned to limited or specific duty—duty that the examiner felt could be handled by the applicant without the danger of low back injury. During the last three years, what with the increased efficiency of the preemployment examinations and the lessons learned from past experience, the number of rejected applicants for employment has increased and the number of persons reporting to sick call with low back injury has decreased. Three years ago 2.2% of the applicants were rejected for employment. Two years ago 3.6% of all applicants were rejected for employment and 12.5% were placed on limited duty. Last year 5.5% of the applicants were rejected for employment and 11.3% were placed on restricted or limited duty.

The coffee company has been providing preemployment examinations of the low back since 1941. During this period they have not had a single serious case of low back injury. Eight employees have reported to the dispensary with low back complaints, with a total loss of 12 work-days; five of these employees were treated in the dispensary and lost no time. A reexamination of the low back x-ray studies of these eight employees taken at the time of employment reveals that seven had negative findings, while one had a slight tilting of the fifth lumbar segment, which could not be called pathological.

TABLE 1.—*X-Ray Findings in 6,523 Preemployment Low Back Examinations*

	%
Congenital anomalies in lumbosacral region	41.1
Normal spines	39.93
Wear-and-tear changes in the lumbosacral joint	6.3
Postural scoliosis	5.0
Advanced spinal arthritis	3.3
Structural scoliosis	1.9
Increased lumbar lordosis	1.3
Old compression fracture of vertebra	0.7
Opaque material in neural canal	0.47

The larger plant operating on war contracts opened in December, 1948, and instituted preemployment low back examinations approximately three years later. During this entire period of operation of approximately six years, 22 claims on low back injuries have been filed with the compensation committee. Many minor back complaints have been treated in the dispensary but have caused no loss of work time. Of the 22 employees whose injuries were listed as compensatory, 6 lost no charged time from work. The remaining 16 have lost a total of 10,036 man-days, and there has been a total financial loss of approximately $34,997 to the company. Only 5 employees of this group of 22 had preemployment examinations. Thus, 17 of these cases of low back injury occurred in individuals who were employed before 1952, while only five employees have reported injured backs since the examinations were instituted. The 17 employees have lost an aggregate of 8,230 man-days and have cost the company or insurance carrier approximately $29,946, while the 5 employees reporting back injuries who had preemployment back examinations have lost 1,806 days at a total cost to the company of $5,050.96. The accounting department of the plant working on war contracts has concluded that the cost of the preemployment examinations is negligible when compared to the dollars and man-days saved.

TABLE 2.—*Comparison of Results of X-Ray Studies in Present Preemployment Examinations with Findings in Series of Patients Who Sought Treatment for Low Back Pain or Disability*

Findings	Preemployment Examinations, %	Low Back Disability Series, %
Congenital anomalies (weak lumbosacral architecture)	41.1	31.1
Arthritis	3.3	15.1
Negative x-ray findings	39.9	13.8
Postural defects	5.0	13.3
Wear-and-tear changes in the lumbosacral joint	6.3	2.3
Others	4.4	24.4

Comment

It is our feeling that back examinations should not be used simply as a means of evaluating the prospective employee. The adolescent should have a careful back examination, including x-rays, to determine any serious congenital architectural defects of the spine. If such defects are found, the individual can be advised to study a profession or trade in order that he may depend upon his brains and not his back for his livelihood. Those applicants for employment who are found to have serious architectural defects of the spine are apprised of the condition. In our series, we found that most applicants were not aware of the weakness. They were cautioned to avoid heavy lifting and straining, not only while at work but in their everyday life. Most of them appreciated this advice.

In order to establish criteria that would be a guide to employment and a basis of job placement, it is hoped that a joint committee of orthopedic and industrial surgeons can be set up to institute and analyze surveys on this subject. Such a committee could, after a correlated study over a sufficient period of time, set up standards for backs that would withstand the rigors of employment just as the ophthalmologist and otolaryngologist have given us standards for eye and ear preemployment examinations. We would suggest that the following information be gathered for analysis: (1) the incidence of lumbosacral anomalies and acquired pathological changes in the low back found at preemployment x-ray examinations; (2) the incidence of work refusal and of limited duty status after preemployment examinations; (3) the comparative loss by the employer of money and man-days under the nonpreemployment examination system and under an efficient system of preemployment examination of the low back; (4) the results of accurate study and comparison of the preemployment records with the x-rays and examination after injury and treatment, to ascertain what types of spines are most liable to break down under

the stress of employment; and (5) the results of careful evaluation of employees who have sustained back injuries and have been treated by conservative or operative methods, to ascertain how these persons will withstand the rigors of reemployment.

Summary

In a series of 6,523 preemployment physical and x-ray examinations, congenital anomalies of the lumbosacral region were found in 41.1% of all persons examined. Only 39.9% of the prospective employees had no abnormal architectural weakness or pathological findings. On the basis of the examination findings, 3.6% of the applicants were refused employment and 12.5% were assigned to a limited duty—duty that the examiner felt the applicant could handle without hazard of back injury. A program of preemployment examinations of the low back or lumbosacral area will conserve money for the employer or insurance carriers as well as eliminate the loss of many man-days of work by the employee. Such a program will act as a warning of future employment hazards and as a basis for job placement. The preemployment records should prove most helpful in the evaluation of subsequent injury and disease and would be of material assistance in the adjudication of medicolegal problems that might arise from injuries received on the job.

4312 J. C. Nichols Parkway (11) (Dr. Diveley).

BODY FLUIDS IN HYPERTENSION AND MILD HEART FAILURE

Lieut. Mackenzie Walser, Lieut. Benedict J. Duffy Jr.
and
Lieut. (j.g.) Henry W. Griffith, (MC), U. S. N. R.

• The intravenous injection of 250 μc of sodium radiosulfate containing S^{35} yields a figure called the radiosulfate space, an estimate of the extracellular water of the body. This figure, divided by the patient's weight, gave 16.1% as the average extracellular water in 30 normal subjects. The average for patients with congestive heart failure without palpable edema was 22.5%.

Simultaneous injection of erythrocytes labeled with 15 μc of radiochromium permitted determination of the blood volume in the same subjects. No significant difference in blood volume was found between the normals and the patients with congestive heart failure without edema.

Calculations based on these facts showed that a patient in mild heart failure might have an increase of 5 liters in extracellular water without palpable edema. Therefore the determination of the radiosulfate space should help in the diagnosis of latent or impending cardiac edema. Uncomplicated hypertension in 11 subjects was not accompanied by demonstrable changes in either blood volume or radiosulfate space.

A reliable and practical method for measuring extracellular fluid would be a great aid in the diagnosis and management of cardiac patients, as well as a useful adjunct to the study of the pathological physiology of congestive failure. A rise in the volume of the extracellular fluid is one of the earliest and most characteristic manifestations of congestive failure, and improvement is almost invariably associated with a fall in extracellular fluid volume toward normal, with accompanying diuresis. In fact, most of the symptoms of congestive failure can be attributed to excess extracellular fluid, either in the lungs or in the periphery.

When large excesses of extracellular fluid are present, they are easily detected by physical examination. A change in the severity of decompensation with an accompanying change in extracellular fluid volume may be noticeable as a change in the fluid level in the chest, the abdominal girth, the amount of swelling of the legs, or the rales heard in the lungs. At best, these physical signs give only a qualitative index of the severity of the fluid retention. The change in body weight during rapid diuresis is a fairly reliable index of the amount of extracellular fluid lost, but, when the weight loss or gain is slow, it is difficult or impossible to distinguish between loss or gain of lean tissue or fat and loss or gain of extracellular fluid. For example, a patient may gain 3 kg. (6.6 lb.) of excess extracellular fluid during a few weeks but lose 3 kg. of tissue and fat at the same time, so that no change in body weight occurs.

When the amount of excess extracellular fluid is slight, the changes in physical signs become even less reliable indexes of the degree of fluid retention, and considerable amounts of excess fluid may escape detection entirely. It is particularly under these circumstances that a measure of extracellular fluid volume would be most useful, both in detecting early congestive failure and in following the progress of congestive failure in patients who do not have manifest edema.

The purpose of the present report was to determine whether useful information could be obtained in patients with congestive failure, using radiosulfate as a measure of the extracellular fluid volume. This substance appeared to offer promise for this purpose because of the ease of analysis [1] and its rapid diffusibility.[2] The observations have been confined to patients without manifest

From the Naval Hospital and Naval Medical Research Institute, Bethesda, Md. Dr. Walser is now at the National Heart Institute, Bethesda, Md. Dr. Duffy is now at Georgetown University, Medical School, Washington, D. C. Dr. Griffith is now at Dade County Hospital, South Miami, Fla.

The opinions expressed herein are those of the authors and do not necessarily reflect the official views of the U. S. Navy or the naval service at large.

1. Walser, M.; Reid, A. F., and Seldin, D. W.: A Method of Counting Radiosulfur in Liquid Samples, and Its Application to the Determination of S^{35} Excretion Following Injection of $S^{35}O_4$, Arch. Biochem. **45**: 91, 1953.

2. Sheatz, G. C., and Wilde, W. S.: Transcapillary Exchange Rate and Volume of Distribution of Sulfate and Sodium as Indicated by $S^{35}O_4$ and Na^{24} in the Rat, Am. J. Physiol. **162**: 687, 1950.

edema for two reasons. In the first place, these subjects are the ones in whom physical examination is least satisfactory in quantitating the amount of fluid retention, and, in the second place, the likelihood of equilibration of the radiosulfate throughout the extracellular fluid of these subjects is much greater. In the presence of marked edema, the equilibration of injected substances is markedly delayed and may require several hours for even the most rapidly diffusing substances, such as water [3] and sodium.[4] Consequently, the determination of extracellular fluid volume in the presence of gross edema is not feasible by the usual dilution techniques.

One of the difficulties in the measurement of body fluids is the selection of a suitable referent. Body weight has been most widely employed but is obviously less than ideal, because the variability of the results of the measurement of total body water, extracellular fluid volume, or blood volume in terms of body weight is great even in healthy young adults. Other referents that have been suggested, such as surface area and height, have not proved to be significantly better.

From a theoretical point of view, it may be argued that the fat-free body weight is the ideal referent. It has been suggested that the fat-free body may contain a fixed proportion of total water, extracellular fluid, and blood and, furthermore, that fat contains very little water. If this were the case, the ratio of extracellular fluid volume to blood volume would be constant. Accordingly, we have investigated the blood volume as a referent for the extracellular fluid volume in normal subjects, that is, extracellular fluid volume has been expressed as liters per liter of blood volume. Since congestive failure may be associated with an increase in the volume of the blood, the use of this ratio might tend to obscure the rise in extracellular fluid volume in patients with congestive failure. However, the use of weight as a referent tends to obscure the rise also, since the volume is related to a weight that includes the increment in extracellular fluid volume. The use of these two referents, weight and blood volume, has therefore been studied in normal subjects and patients with congestive failure. Grollman [5] has reported that hypertension is associated with a rise in the extracellular fluid volume, as measured by the radiosulfate space. We have accordingly included a group of subjects with hypertension but no cardiac decompensation.

Methods

Extracellular fluid volume was estimated by means of radiosulfate,[6] and blood volume was determined with radiochromium-labeled erythrocytes.[7] These two isotopes, S^{35} and Cr^{51}, may be determined in the same sample of blood without interference; thus it was possible to make the two measurements simultaneously. The detailed procedure follows. A sample of the patient's blood was labeled with Cr^{51} according to the technique of Sterling and Gray.[7] A sterile solution of S^{35}-labeled sulfate, carrier-free, in sodium chloride solution was prepared; 250 μc of this solution was injected intravenously. Ten minutes later 15 μc of the Cr^{51}-labeled erythrocytes was injected. Ten minutes after this a 15 ml. sample of blood was obtained in a syringe containing heparin. Cr^{51} was determined on whole blood in a well-type scintillation counter. Blood volume was calculated as the counts injected divided by the counting rate of the blood sample. Though hematocrit determinations were done, the data are not included since the conclusions to be drawn are not dependent upon disparate changes in plasma volume and red blood cell mass. However, since the hematocrit of the venous blood sample obtained probably differed from the body hematocrit,[8] the figures reported for blood volume may include a constant or possibly variable error. The significance of this possible error is discussed below.

S^{35} was determined directly in plasma in a specially constructed cup designed for liquid counting of weak beta emitters.[1] A flow counter was used. The radioactivity of the injected solution, diluted in normal plasma, was determined simultaneously. The volume of distribution of radiosulfate was calculated as follows:

$$V_d = \frac{\text{Counts injected} \times 0.95}{\text{Counts in plasma} / (0.90 \times 0.93)} = 0.8 \frac{\text{Counts injected}}{\text{Counts in plasma}}.$$

The number 0.95 represents a correction for radiosulfate excreted during the 20 minute equilibration period; 5% loss is an average value for normal persons [6]; 0.90 represents a correction for the Donnan factor for sulfate; and 0.93 is a correction for the water content of plasma, which is assumed to be normal.

The subjects have been divided into three groups: normal subjects, hypertensive patients without congestive failure, and subjects with congestive failure but no clinical edema. The criteria for selection of these three groups were as follows: (1) normal subjects: ambulatory, healthy persons with no complaints, no recent major illness or operation, and no recent loss or gain of more than 10 lb. (4.5 kg.) of weight; (2) hypertensive patients: (*a*) sustained diastolic pressure above 90 mm. Hg, even after two weeks in the hospital, (*b*) normal basal metabolic rate, intravenous pyelogram, and regitine test (all of these tests were not performed in each subject, but, when omitted, the clinical evidence was felt to make the test unnecessary; most subjects had two of three tests), (*c*) absence of other illness of possible effect upon body fluids, (*d*) no exertional dyspnea, orthopnea, rales, hepatomegaly, distended neck veins, or peripheral edema and no pulmonary congestion on x-ray, and (*e*) normal blood urea nitrogen or nonprotein nitrogen concentration (not more than 20 mg. per 100 cc. of albumin in urine and no more than a few red or white

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7. Sterling, K., and Gray, S. J.: Determination of the Circulating Red Cell Volume in Man by Radioactive Chromium, J. Clin. Invest. **29**: 1614, 1950.

8. (*a*) Chaplin, H., Jr.; Mollison, P. L., and Vetter, H.: The Body/Venous Hematocrit Ratio: Its Constancy over a Wide Hematocrit Range, J. Clin. Invest. **32**: 1309, 1953. (*b*) Schreiber, S. S.; Bauman, A.; Yalow, R. S., and Berson, S. A.: Blood Volume Alterations in Congestive Heart Failure, ibid. **33**: 578, 1954. (*c*) Hedlund, S.: Studies on Erythropoiesis and Total Red Cell Volume in Congestive Heart Failure, Acta med. Scandinav. (supp. 284) **146**: 1, 1953.

blood cells in sediment); (3) congestive failure patients: (*a*) exertional dyspnea, (*b*) venous pressure above 90 mm. H_2O, and (*c*) no peripheral edema. All measurements were made at least two and one-half hours after

TABLE 1.—*Replicate Determinations of Extracellular Fluid Volume (Radiosulfate) and Blood Volume (Radiochromium-Labeled Cells)*

Subject	Date	ECF,* Liter	BV,† Liter	% Change in ECF	% Change in BV
A	1/ 8/54	14.6	4.82		
	1/20/54	13.8	4.74	4	2
B	3/ 8/54	11.5	3.53		
	3/23/54	11.7	3.68	2	5
C	3/ 8/54	12.2	3.40		
	3/23/54	12.5	3.66	3	8
D	3/10/54	11.3	4.54		
	3/22/54	10.3	4.42	9	2
	3/29/54	10.8	....	5	..

* ECF = extracellular fluid volume.
† BV = blood volume.

quently, since the isotope is almost entirely excreted within a few days [1] and the radiation dosage is small.[6] Since Cr^{51} remains within the erythrocyte throughout its life span, it is not possible to repeat this procedure as often. Three determinations within three weeks are a safe limit with this dosage (15 μc). The reasons for believing that radiosulfate equilibrates throughout the diffusible portion of the extracellular fluid within 20 minutes in normal subjects have been given elsewhere.[9] In the presence of disease, the rate of equilibration may well be altered (see above). However, the use of single blood samples obtained after a greater interval to calculate the extracellular fluid volume is hazardous since radiosulfate penetrates cells.[6] The use of multiple sampling of blood and urine makes it possible to circumvent this but is not feasible clinically. Consequently, the single 20-minute sample was obtained in all the subjects.

TABLE 2.—*Extracellular Fluid Volume (Radiosulfate) and Blood Volume (Radiochromium) in Normal Ambulatory Subjects*

Sex	Age, Yr.	Height, Cm.	Weight, Kg.	ECF,‡ Liter	BV,§ Liter	ECF, Liter/Kg. × 100	BV, Liter/Kg. × 100	ECF/BV, Ratio	SA,‖ Sq. M.	ECF, Liter/ Sq. M.	BV, Liter/ Sq. M.
M	17	175	62.3	11.3	4.54	18.1	7.29	2.49	1.76	6.42	2.58
M	18	183	85.4	12.2	....	14.3	....	....	2.08	5.86	....
M	19	170	70.2	13.0	4.86	18.5	6.92	2.67	1.81	7.18	2.69
M	19	183	79.3	13.6	4.12	17.2	5.20	3.30	2.01	6.77	2.05
M	19	193	88.6	16.0	6.23	18.1	7.03	2.57	2.20	7.27	2.83
M	20	167	54.5	10.3	3.78	18.9	6.94	2.72	1.61	6.40	2.35
M	20	178	73.6	12.2	5.36	16.6	7.28	2.28	1.90	6.42	2.82
M	20	145	77.3	13.3	5.25	17.2	6.79	2.53	1.69	7.87	3.11
M †	20	183	100.5	14.0	5.77	13.9	5.74	2.43	2.23	6.28	2.59
M	20	173	72.7	14.1	....	19.4	....	....	1.86	7.58	....
M	20	178	101.9	11.6	5.06	11.4	4.96	2.29	2.19	5.30	2.31
M	20	180	79.0	11.2	6.06	14.2	7.67	1.85	1.98	5.66	3.06
M *	21	178	85.5	15.9	5.09	18.6	5.95	3.12	2.03	7.83	2.51
M	22	178	70.2	10.8	4.86	15.4	6.92	2.22	1.87	5.78	2.60
M	22	185	78.6	11.9	....	15.1	....	....	2.02	5.89	....
M	23	193	86.8	15.5	6.37	17.9	7.34	2.43	2.18	7.11	2.92
M	23	180	88.0	11.6	4.29	13.2	4.88	2.70	2.08	5.78	2.06
M	23	176	65.2	11.8	4.05	18.1	6.21	2.91	1.80	6.56	2.25
M †	24	184	92.5	15.4	5.45	16.6	5.89	2.82	2.15	7.16	2.53
M †	24	182	79.5	14.2	4.76	17.9	5.99	2.98	2.01	7.06	2.37
M	24	179	78.1	10.3	....	13.2	....	....	1.97	5.23	....
M	25	178	83.6	13.0	4.39	15.6	5.25	2.96	2.00	6.50	2.19
M	26	183	86.4	15.1	5.51	17.5	6.38	2.74	2.08	7.26	2.65
M	32	165	59.8	10.9	3.93	18.2	6.57	2.77	1.66	6.57	2.37
M *	35	180	75.5	13.5	4.29	17.9	5.68	3.15	1.94	6.96	2.21
M	40	185	84.1	13.9	....	16.5	....	....	2.08	6.68	....
F *	42	172	58.6	8.6	....	14.7	....	....	1.70	5.06	....
M *	43	168	75.0	10.2	5.34	13.6	7.12	1.91	1.84	5.54	2.90
M	46	...	53.6	8.5	3.28	15.9	6.12	2.59	....	....	....
M	47	178	82.2	11.9	4.76	14.5	5.79	2.50	2.00	5.95	2.38
M	64	180	75.9	10.5	4.38	13.8	5.77	2.40	1.95	5.38	2.25
F *	70	137	54.7	7.6	....	13.9	....	....	1.39	5.47	....
Mean						16.1	6.31	2.61	....	6.41	2.52
Standard deviation						2.1	0.78	0.35	....	0.79	0.30
Coefficient or variation						0.13	0.12	0.13	....	0.12	0.12

* Mean of two determinations. † Mean of three determinations. ‡ ECF = extracellular fluid volume.
‖ SA = surface area. § BV = blood volume.

the last meal. Venous pressure was determined with the patient lying flat, after a 15-minute rest in bed. The measurements were all made by us, using a standardized technique.

Results

The reproducibility and precision of these techniques may be seen in table 1. The average error of a single determination by either method appears to be about 5%. The radiosulfate determination may be made fre-

Normal Subjects.—The results of simultaneous measurement of extracellular fluid volume and blood volume in normal subjects are shown in table 2. The subjects have been placed in order of ascending age. The ratio of extracellular fluid to blood volume has been calculated for each subject. The mean ratio, 2.61, indicates that the ratio of extracellular fluid to plasma volume was about 4.6; i. e., approximately 80% of the readily diffusible extracellular fluid lies outside of the circulation. This figure is in accord with previous estimates. The variability of this ratio, extracellular fluid to blood volume, is just as great as the variability of extracellular

9. Ryan, R. J.; Inouye, T., and Bernstein, L.: The Zero Time Radiosulfate Space in Normal and Abnormal Subjects, J. Lab. & Clin. Med. 44:923, 1954. Footnote 6.

fluid per kilogram of body weight. This is surprising since one would expect that lean subjects would have a large amount of extracellular fluid and blood per unit weight and subjects with a large percentage of fat would have a small amount of extracellular fluid and blood per unit weight. In extremely obese subjects this appears to be the case, but in subjects selected at random the factors determining extracellular fluid and blood volume are evidently different and induce as much variability in the ratio of the one to the other as lean body weight induces in either one alone. The use of surface area as a referent, shown in the last two columns, provides no advantage. The coefficient of variation of extracellular fluid is about the same, no matter which referent is chosen.

TABLE 3.—*Extracellular Fluid Volume (Radiosulfate) and Blood Volume (Radiochromium-Labeled Cells) in Hypertensive Patients Without Renal or Cardiac Failure*

Sex	Age, Yr.	Height, Cm.	Weight, Kg.	ECF,* Liter	BV,† Liter	ECF, Liter/ Kg. × 100	BV, Liter/ Kg. × 100	ECF/ BV, Ratio
M	22	174	77.3	10.6	4.40	13.7	5.69	2.40
M	23	173	77.3	12.6	4.10	16.3	5.30	3.07
M	23	174	76.4	14.8	4.36	19.4	5.70	3.40
M	30	173	92.3	17.1	6.68	18.4	7.20	2.56
F	33	160	53.6	9.1	3.07	17.0	5.74	2.96
M	35	179	80.2	12.9	....	16.1	....	....
M	40	179	77.3	11.5	4.79	14.9	6.20	2.40
M	56	179	93.0	11.5	5.98	12.4	6.43	1.92
M	60	162	65.9	10.0	....	15.2	....	....
M	61	163	66.8	10.8	3.61	16.2	5.40	2.99
M	64	168	83.2	15.9	4.10	19.1	4.93	3.88
Mean						16.2	5.84	2.84
Standard deviation						2.1	0.67	0.58

* ECF = extracellular fluid volume.
† BV = blood volume.

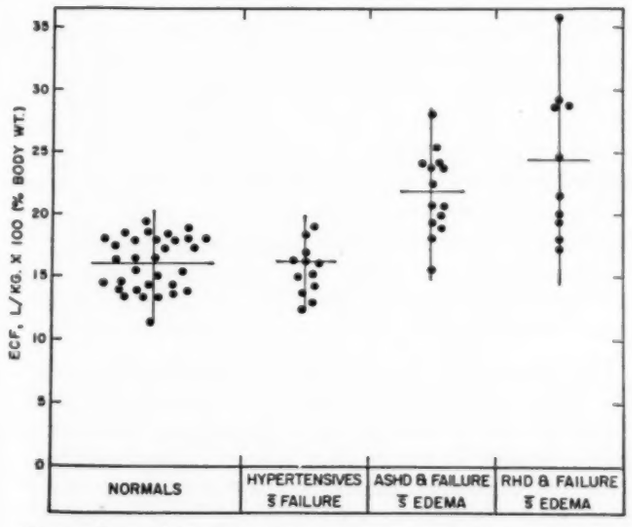

Fig. 1.—Extracellular fluid (radiosulfate space) in relation to weight in normal patients, hypertensive patients, and patients with arteriosclerotic and rheumatic heart disease and congestive failure.

Hypertensive Patients.—The results in hypertensive subjects are shown in table 3 and in figures 1, 2, and 3. No significant difference between these subjects and the normal controls was found. However, in view of the wide range of normal values and the small number of cases, it is possible that a small increase in hypertension may not have been detected. This is suggested by the greater mean ratio, extracellular fluid to blood volume, in this group, although this difference is not statistically significant. It must be emphasized that these patients were all thoroughly evaluated in the hospital both to ascertain the presence of sustained diastolic hypertension and to exclude the presence of other complicating conditions, including cardiac or renal failure.

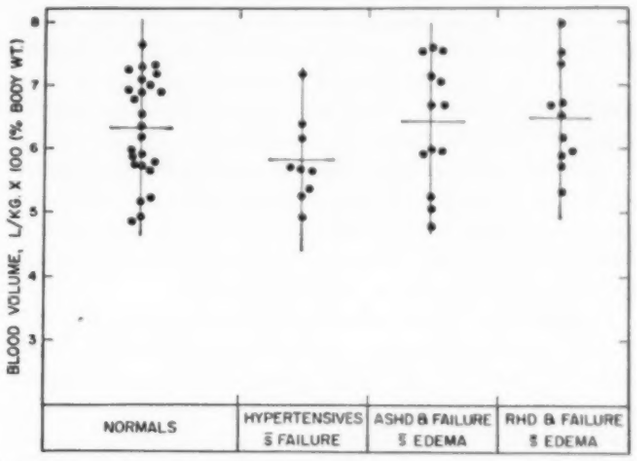

Fig. 2.—Blood volume (radiochromium-labeled erythrocytes) in relation to weight in normal patients, hypertensive patients, and patients with arteriosclerotic and rheumatic heart disease and congestive failure.

Congestive Failure Patients.—Congestive failure patients, numbering 24 in all, have been divided into two groups: those with arteriosclerotic heart disease (which includes some who had hypertension in addition to coronary atherosclerosis) and those with rheumatic heart disease. This distinction was made because of reports that blood volume is greater in patients with rheumatic heart disease.[10] However, the differences between the subjects with rheumatic heart disease and those with arteriosclerotic heart disease were slight and probably insignificant.

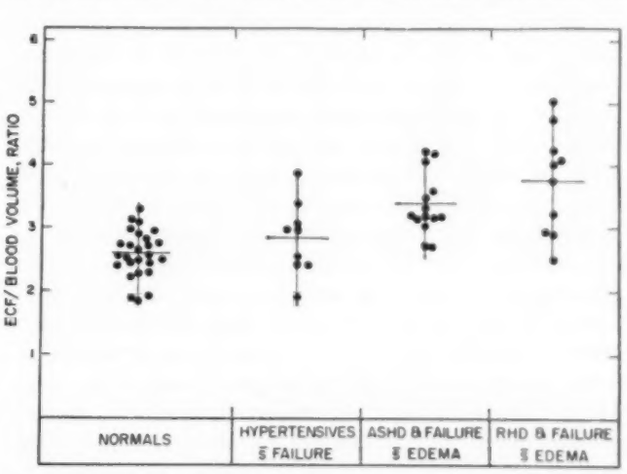

Fig. 3.—Ratio of extracellular fluid volume to blood volume in normal patients, hypertensive patients, and patients with arteriosclerotic and rheumatic heart disease and congestive failure.

As indicated in tables 4 and 5, all of these subjects had increased peripheral venous pressure and many had prolonged circulation time. There was little correlation

10. Prentice, T. C., and others: Total Red Cell Volume, Plasma Volume, and Sodium Space in Congestive Heart Failure, J. Clin. Invest. **30**: 1471, 1951.

between the degree of elevation of the venous pressure, the prolongation of the circulation time, and the extracellular fluid volume. The mean extracellular fluid volume in the patients with arteriosclerotic heart disease was 21% of body weight, and the mean in the patients with rheumatic heart disease was 24% of body weight. These values both differ significantly from the normal mean of 16%. When expressed in terms of blood volume, the results are very similar, as shown in figure 1 and figure 3. Of the 24 subjects in all with congestive failure, 17, or 72%, have a value for extracellular fluid in relation to weight that is above the upper limit of the normal range, 19%. The mean increase for the entire group is 5 liters of extracellular fluid, being slightly greater in the subjects with rheumatic heart disease. Figure 3 shows that, even in the absence of edema, the increase in extracellular fluid volume is proportionately much greater than the increase in blood volume.

Comparison of the blood volume values for the four groups of subjects shows no significant differences: normal subjects, 63.1 ml. per kilogram; patients with hypertension, 58.4 ml. per kilogram; patients with arteriosclerotic heart disease in failure, 62.8 ml. per kilogram; and patients with rheumatic heart disease in failure, 66.8 ml. per kilogram. However, it is also possible here that a true difference between normal subjects and those in failure exists but cannot be detected by comparing small groups. Furthermore, the subjects with congestive failure had an average of 5 kg. of excess weight, so that their blood volumes expressed in terms of their edema-free weight would have been about 8% larger.

Repeated measurements of radiosulfate space and of blood volume were made during the course of hospitalization in several patients with heart failure but without edema. Some representative results are shown in table 6. The first subject responded rapidly to conventional therapy, and within 11 days his venous pressure and circulation time were normal and he was asymptomatic at rest. His improvement was associated with a loss of 6.8 kg. (15 lb.) of weight and 4.7 liters of measured extracellular fluid. His blood volume did not change in absolute amount, but, because of the loss of weight, the blood volume per kilogram increased from 50.8 ml. to 57.0 ml. The next two subjects both failed to achieve compensation despite therapy. The first case was complicated by chronic bronchopulmonary infection and the second by obesity. In these and other subjects, the blood volume changes, although not of great magnitude, were entirely unpredictable. The radiosulfate space changes appeared to reflect the clinical state more accurately than either blood volume or venous pressure. However, this observation is at best a clinical impression, since there is no satisfactory quantitative measure of the severity of heart failure. Our observations on blood volume before and after therapy for congestive heart failure are too few and too variable to permit any conclusions to be drawn concerning the effect of congestive heart failure upon the blood volume. Several papers on this subject have appeared recently.[11]

Comment

The clinical value of radiosulfate space in patients with congestive failure cannot be determined finally from these observations. A limited number of subjects has been studied, and insufficient observations of radiosulfate space have been made in other conditions. Obviously an increase in radiosulfate space is not specific for congestive failure, but, in addition to the conditions that are known to be associated with a rise in extracellular fluid volume besides congestive failure, there may well be others as yet unrecognized in which an elevation in extracellular fluid volume is the rule rather than the exception but that seldom progress to the stage of manifest edema. Among the conditions in which it has been suggested that extracellular fluid may be increased but that rarely are associated with manifest edema are acute rheumatic fever [12] and metabolic alkalosis.[13] Further data in these and other conditions are needed.

The present data do show that a measurable increase in extracellular fluid volume occurs in congestive heart failure before edema becomes manifest. That several liters of excess interstitial fluid may be present without palpable edema is not surprising, but the regularity with which radiosulfate space is increased was unexpected. Of the 24 subjects with heart failure, only 7 had a radiosulfate space in relation to weight that fell within the normal range. In view of the rather wide range of normal values, this result is rather surprising.

These results also demonstrate the preeminence of the expansion of interstitial fluid volume over the expansion of blood volume in early heart failure. Retained salt and water accumulate in the interstitial space much more readily than in the plasma [14] for reasons as yet unknown. One may speculate that the change in venous pressure produced by a 10% rise in blood volume is much greater than the change in interstitial fluid pressure produced by a proportionate rise in the total extracellular fluid volume. This would explain the fact that the great majority of the retained fluid is found outside of the blood stream.

The assumption has been made throughout this paper that blood volume can be calculated from the measured red blood cell mass and the hematocrit of the venous blood. Studies in which plasma volume has been independently measured simultaneously with the measurement of the volume of red blood cells have shown that the average hematocrit of the circulating blood is about 10% lower than the venous hematocrit.[8] Consequently, the blood volumes calculated herein are probably slightly lower than the true volumes. The difference between body hematocrit and venous hematocrit is apparently not affected by anemia [8a] but may increase in cardiac decompensation,[8b] although others have reported that it does not.[8c] Because of this conflicting evidence, we have made no attempt to correct for the difference between venous hematocrit and body hematocrit. It is well

11. Eisenberg, S.: The Effect of Congestive Heart Failure on the Blood Volume as Determined by Radiochromium-Tagged Red Cells, Circulation **10**: 902, 1954.

12. (*a*) Aikawa, J. K.: The Cell Membrane Defect in Acute Rheumatic Fever, North Carolina M. J. **13**: 330, 1952. (*b*) Walser, M.; Duffy, B. J., Jr., and Griffith, H. W.: Observations on the Radiosulfate Space in Disease, abstracted, Clin. Res. Proc. **3**: 126, 1955.

13. Roberts, K. E.; Randall, H. T.; Philbin, P., and Lipton, R.: Changes in Extracellular Water and Electrolytes and the Renal Compensations in Chronic Alkalosis, as Compared to Those Occurring in Acute Alkalosis, Surgery **36**: 599, 1954.

14. Walser, M.; Seldin, D. W., and Burnett, C. H.: Blood Volume and Extracellular Fluid Volume During Administration of ACTH and Cortisone, Am. J. Med. **18**: 454, 1955.

to emphasize that an increase in plasma volume in congestive failure that is not reflected in a fall in venous hematocrit, i. e., that involves only the small vessels, would not be detected by the chromium-51 method.

The results in the small group of hypertensive subjects do not lend support to the conclusions of Shapiro and Grollman [5a] and Teng, Shapiro, and Grollman [5b] that radiosulfate space is increased in hypertension. However, on examining their data and ours in detail, it becomes evident that the demonstration of a rise in radiosulfate space in hypertensive patients can only be made under the most favorable circumstances. The normal subjects and hypertensive subjects differ by only 10% in the series reported by Teng and co-workers, or by about 1 liter. Since the standard deviation of normal values is greater than 1 liter, one must rely heavily on statistical methods to establish the significance of such a difference. By selecting a larger proportion of older subjects and of females in order to make the groups comparable, these authors showed a significant though small difference. Their normal subjects differ significantly from those reported herein (mean radiosulfate space = 13.6% of body weight, as opposed to 16.1%), but their hypertensive subjects do not differ significantly

TABLE 4.—*Extracellular Fluid Volume (Radiosulfate) and Blood Volume (Radiochromium-Labeled Red Blood Cells) in Patients With Heart Failure Due to Arteriosclerotic Heart Disease (With and Without Hypertension) but Without Peripheral Edema*

Sex	Age, Yr.	Height, Cm.	Weight, Kg.	VP,* Mm. H_2O	CT,† Sec.	ECF,‡ Liter	BV,§ Liter	ECF, Liter/Kg. × 100	BV, Liter/Kg. × 100	ECF/BV, Liter/Liter
M	46	158	56.4	91	..	13.4	4.04	23.8	7.17	3.32
M	58	179	77.3	160	..	14.8	4.65	19.2	6.02	3.18
M	58	171	81.6	100	18	15.3	4.88	18.8	5.98	3.14
M	59	173	77.3	96	27	16.0	3.93	20.7	5.08	4.07
M	60	169	53.6	140	..	12.7	3.64	23.7	6.80	3.49
M	60	175	72.7	120	22	15.0	5.55	20.7	7.64	2.70
M	61	178	63.6	120	..	12.6	3.83	19.8	6.02	3.29
M	63	...	52.7	...	..	9.5	3.13	18.0	5.94	3.03
M	63	173	97.7	153	21	15.2	4.79	15.6	4.80	3.16
M	74	158	61.8	92	10	14.9	4.68	24.1	7.57	3.18
M	77	173	64.5	143	25	16.4	4.57	25.4	7.08	3.58
F	83	165	72.0	126	..	16.1	3.81	22.4	5.29	4.22
Mean								21.0	6.28	3.36
Standard deviation								2.9	0.96	0.43

* VP = venous pressure. † CT = circulation time. ‡ ECF = extracellular fluid volume. § BV = blood volume.

TABLE 5.—*Extracellular Fluid Volume (Radiosulfate) and Blood Volume (Radiochromium-Labeled Red Blood Cells) in Patients With Heart Failure Due to Rheumatic Heart Disease Without Peripheral Edema*

Sex	Age, Yr.	Height, Cm.	Weight, Kg.	VP,* Mm. H_2O	CT,† Sec.	ECF,‡ Liter	BV,§ Liter	ECF, Liter/Kg. × 100	BV, Liter/Kg. × 100	ECF/BV, Liter/Liter
F	19	162	46.8	120	18	10.0	2.50	21.5	5.34	4.00
M	23	168	52.3	185	16	18.7	3.95	35.8	7.56	4.74
F	29	173	49.5	110	14	8.5	2.92	17.2	5.90	2.91
F	36	156	45.9	146	20	11.0	3.60	24.0	7.85	3.06
F	38	165	48.0	140	..	9.3	2.88	19.4	5.98	3.24
F	43	165	47.7	158	26	13.4	3.20	28.1	6.71	4.19
M	44	178	58.1	86	15	12.6	4.29	20.7	7.38	2.94
F	45	170	53.6	100	16	15.4	3.08	28.8	5.75	5.00
M	45	172	63.9	192	52	15.7	4.18	24.6	6.56	3.75
M	49	...	62.5	180	60	12.5	5.00	20.0	8.00	2.50
M	49	182	77.9	147	20	14.0	4.82	18.0	6.20	2.90
F	52	...	43.2	118	18	12.6	2.97	29.2	6.87	4.24
Mean								23.9	6.68	3.62
Standard deviation								5.6	0.87	0.62

* VP = venous pressure. † CT = circulation time. ‡ ECF = extracellular fluid volume. § BV = blood volume.

TABLE 6.—*Serial Measurements of Extracellular Fluid Volume (Radiosulfate) and Blood Volume (Radiochromium) in Patients with Congestive Failure*

Subject	Diagnosis	Date	Weight, Kg.	VP,* Mm. H_2O	CT,† Sec.	ECF,‡ Liter	BV,§ Liter	Remarks
1	Aortic stenosis in early failure, untreated	1/15	77.3	96	27	16.0	3.93	Rales and dyspnea
		1/26	70.5	70	20	11.3	4.02	Compensated on digitalis and low-salt diet
2	Coronary artery disease in failure 12 yr., hypertension and bronchitis	1/26	64.5	60	25	16.4	4.57	Dyspnea, cough, and rhonchi; unimproved despite increased digitalis
		2/8	69.5	143	17	14.7	5.35	
3	Coronary artery disease, hypertension, and obesity	2/9	97.7	153	21	15.2	4.79	Untreated
		2/12	95.5	112	20	14.2	5.12	Digitalized
		2/19	94.5	113	17	14.8	....	Unchanged
		2/23	94.3	180	17	22.1	5.23	Dyspnea increased

* VP = venous pressure. † CT = circulation time. ‡ ECF = extracellular fluid volume. § BV = blood volume.

from ours nor from our normal subjects. In conclusion, it may be stated that the elevation in radiosulfate space in hypertension is slight and trivial in comparison to the elevation that occurs in early congestive failure. It is likely that the elevation found in some hypertensive subjects may be due to early and as yet asymptomatic cardiac impairment.

Summary

The extracellular fluid and blood volume in 24 subjects with congestive failure but no edema and in 11 subjects with uncomplicated hypertension have been compared to that in 32 normal subjects. Extracellular fluid volume, estimated with radiosulfate, and blood volume, estimated with radiochromium-labeled cells, can be determined simultaneously with a single blood sample with a fair degree of precision. In the normal subjects, weight, surface area, and blood volume were compared as referents for extracellular fluid volume. The coefficient of variation was the same with all three referents, 12%. Consequently weight was employed. The mean extracellular fluid volume was 16.1% of body weight in normal subjects, 22.5% in subjects with heart failure but no edema, and 16.2% in hypertensive patients. Seventy-two per cent of the subjects with heart failure had an abnormal value for extracellular fluid volume and the mean increase was 5 liters of fluid despite the absence of palpable edema. The blood volume did not differ significantly in the three groups. Serial measurements in patients with heart failure showed that radiosulfate space fell toward normal with compensation or remained elevated if compensation failed to occur. The data indicate that radiosulfate space may be a valuable index of the severity of heart failure when edema is absent.

ARTIFICIAL RESPIRATION VIA THE UNCUFFED TRACHEOSTOMY TUBE

Ernst Trier Mörch, M.D., Ph.D., George A. Saxton Jr., M.D.
and
Gareth Gish, M.S., Chicago

In the past, intermittent positive-pressure breathing via the tracheostomy tube has been used in patients with acute anterior poliomyelitis in one of two ways: (1) as a supplement to other respiratory equipment (tank respirator, chest respirator, or rocking bed) or (2) as the only means of artificial respiration. The former application has been practiced chiefly in the United States,[1] whereas the latter has been practiced in a few cases in the United States and is the technique commonly used in the Scandinavian countries.[2]

For the administration of intermittent positive-pressure breathing as the only means of artificial respiration, an airtight system has in the past been used almost exclusively except in the series presented here. This is commonly achieved by the use of an inflatable cuff around the distal part of the tracheostomy tube, a technique used for the first time on a wide scale during the 1952 epidemic in Copenhagen (fig. 1). At that time some 300 patients were treated by intermittent positive-pressure breathing given manually over three months, day and night, until mechanical devices were made available. Such devices were made as a result of the epidemic, of which the Engström respirator is the most commonly used in Europe.[3] This respirator requires a closed system and does not work properly if a leak occurs.

• The ordinary Chevalier Jackson silver tracheostomy tube, without inflatable cuff, is easier to insert than is the soft rubber tube with inflatable cuff. The silver tube offers less resistance, the depth of its insertion is better controlled, there is no worry about the possibility of gradual deflation, and there is less danger of trauma to the tracheal mucosa from the constant pressure of the cuff.

The silver tube must be used with a high-capacity, intermittent positive-pressure respirator that can compensate for the leakage up through the larynx. Five makes of respirator have been found usable in this connection. The leak protects against excessive pressure in the lungs and blows pharyngeal secretions up toward the mouth.

The air supplied must be humidified. Accidental disconnections must be prevented. The tracheotomy per se has hazards and complications, but when it is required there are advantages in eliminating the tank respirator and using positive-pressure respiration.

Types of Tracheostomy Tubes

Cuffed Tracheostomy Tube.—Use of the cuffed tracheostomy tube is disadvantageous in many respects, and it is said to be attended by "all sorts of complications."[4] 1. The soft rubber tracheostomy tube with the inflatable cuff is much more difficult to insert into the right place in the trachea than the silver tube. The cuffed tube may go into a via falsa outside the trachea in the loose connective tissue during the first days after the operation; it may not be inserted far enough; or it may be inserted too far, so that it enters the right main bronchus.

Professor of Surgery and Director of Anesthesia, University of Chicago (Dr. Mörch); Associate Professor of Medicine and Director of the Respirator Center, University of Illinois College of Medicine (Dr. Saxton); and Inhalation Therapist, Research and Educational Hospitals, University of Illinois (Mr. Gish).

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1. The Diagnosis and Treatment of the Acute Phase of Poliomyelitis and Its Complications, Bower, A. G., editor, Baltimore, Williams & Wilkins Company, 1954.

2. Lassen, H. C. A.: Preliminary Report on 1952 Epidemic of Poliomyelitis in Copenhagen with Special Reference to Treatment of Acute Respiratory Insufficiency, Lancet **1**: 37, 1953.

3. Engström, C. G.: Respirator Designed According to a New Principle, Svenska läk.-tidning. **50**: 545, 1953.

4. Andersen, E. W., and Ibsen, B.: The Anaesthetic Management of Patients with Poliomyelitis and Respiratory Disease, Brit. M. J. **1**: 786, 1954.

2. The cuff offers resistance on insertion and may rupture or be dislocated during insertion. 3. The cuff is unreliable and treacherous because it is difficult to keep inflated. 4. The inflated cuff presses against the tracheal mucosa and may cause trauma or even necrosis.

Uncuffed Tracheostomy Tube.—The uncuffed tracheostomy tube for intermittent positive-pressure breathing was first used by one of us (E. T. M.) at the University of Kansas Medical Center in 1951, i. e., one year before the Danish epidemic.[5] It proved to be satisfactory if a high-capacity respirator were used, enabling one to compensate for the leak (fig. 2). At first it seemed unreasonable that such an open system could be effective, but as a matter of fact it worked satisfactorily in all cases tried. It has now been used successfully in approximately 22 patients as the only means of artificial respiration. In 10 cases of respiratory paralysis due to central nervous system trauma, neurosurgery, myasthenia gravis, or barbiturate poisoning, the patients have been treated effectively for a few days or weeks at a time. It has also been used continuously for longer periods of time in the management of 12 cases of respiratory paralysis due to poliomyelitis; the last 2 cases are presented here.

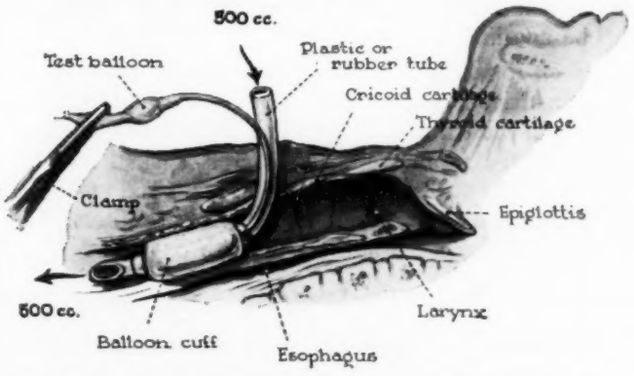

Fig. 1.—Cuffed tracheostomy tube must be airtight in order that all volume delivered to tube enters lungs.

Report of Cases

CASE 1.—A 13-year-old girl was admitted with acute anterior poliomyelitis. On the third day complete paralysis of all four extremities, intercostal muscles, and most of the diaphragm had developed. A chest respirator was tried but found to be inadequate. Marked acidosis developed as indicated by a venous carbon dioxide content of 36.1 mM. per liter and a pH of 7.15. On the fourth day tracheotomy was performed and intermittent positive-pressure breathing started by use of the Mörch piston respirator. From then on a mild respiratory alkalosis was maintained, except on the seventh day, when obstruction of the left bronchus occurred. On the 12th hospital day the chest respirator was again tried. After one hour the patient showed clinical signs of carbon dioxide narcosis, with hallucinations, circulatory collapse, and semicoma. She was returned to the Mörch respirator, and 30 minutes later she was conscious and quite well. The acidosis had disappeared, as indicated by a venous carbon dioxide content of 27.4 mM. per liter and pH 7.43 (fig. 3).

Small atelectases developed repeatedly and were treated by aspiration and postural drainage. The trachea and bronchi were aspirated and washed with 2 ml. of Alevaire (a mixture of 0.125% oxyethylated tertiary octylphenolformaldehyde polymer, 5% glycerin, 2% sodium bicarbonate, and water) in saline solution (1:4) several times per hour. The chest was auscultated several times daily and x-rays taken repeatedly. During the first month serous crusts formed rapidly around the tracheostomy tube, so that it had to be changed every 24 to 36 hours. On the 29th day a Monaghan positive-pressure respirator was utilized because the Mörch respirator was needed for another patient (case 2). On the 31st day she was able to breathe spontaneously for one-half to two minutes by means of the diaphragm; on the 35th day intercostal activity became evident. On the 59th day the patient was placed on a rocking bed for 20 minutes. On the 66th day she could breathe without any artificial aid. On the 71st day the tracheostomy tube was removed and respiration improved markedly. On the 78th day she started to stand and walk. On the 100th day she could get out of a wheel chair without assistance. She was discharged on the 103rd day.

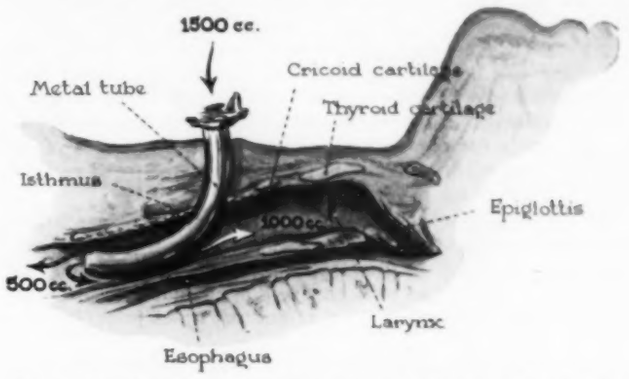

Fig. 2.—Uncuffed tracheostomy tube permits some air to leak through larynx. This leak must be compensated for by delivery of larger volume to tube.

CASE 2.—A 30-year-old man was admitted with acute anterior poliomyelitis. Respiration was effortless at first; the vital capacity was 2 liters. Thirteen hours after admission paralysis of the arms progressed and difficulty in breathing increased; vital capacity was 1.4 liters. On the second day vital capacity equalled 0.6 liter, and the respiratory rate was 44 per minute. A Monaghan chest respirator was applied. Right sternocleidomastoid and trapezius muscles became paralyzed; no other evidence of bulbar involvement was found. Due to an unusual shape of the patient's chest, it was difficult to fit the chest respirator on him; in spite of padding, decubitus ulcer developed over the upper chest and all the way around the chest piece to the iliac crests.

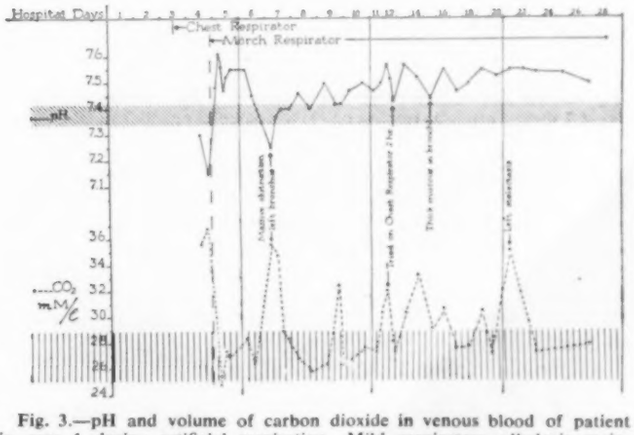

Fig. 3.—pH and volume of carbon dioxide in venous blood of patient in case 1 during artificial respiration. Mild respiratory alkalosis maintained.

On the fifth day increasing respiratory difficulties developed; tracheotomy was performed, and intermittent positive-pressure breathing with a Mörch piston respirator was begun (fig. 4). Dyspnea then disappeared. Repeated episodes of atelectases, mainly in the left side, were treated by postural drainage by turning the patient from side to side and by washing with Alevaire–saline solution (1:4) and aspiration. The air pumped into the lungs

5. Baumeister, J.; Blood, M. J.; Marsh, A., and Roth, A.: Use of Tracheotomy, Intermittent Positive Pressure and Sedation in Treatment of Children Ill with Poliomyelitis, J. Kansas M. Soc. 53: 280, 1952.

was humidified and oxygenated, which seemed to help considerably. Crusts formed outside and at the end of the tracheostomy tube so that it had to be changed one or more times daily for the first two months. By the 63rd day the patient was able to take 60 breaths spontaneously using the accessory muscles in the neck. On the 87th day he could breathe for 11 minutes. On the 96th day the vital capacity was 170 ml.; on the 117th day it was 290 ml., with a minute volume of 7.25 liters. On the 100th day the patient was placed on a rocking bed for a few minutes at a time. On the 163rd day his vital capacity was 350 ml. On the 183rd day he was transferred to a respirator center with complete paraplegia and essentially no function in the right leaf of the diaphragm or intercostal muscles. He was able to breathe spontaneously for one and one-quarter hours by means of his accessory respiratory muscles in the neck and the small residual in the left leaf of the diaphragm.

At the respirator center the Monaghan pressure attachment was substituted for the Mörch respirator. Then, in order to help him raise secretions by rocking, a Monaghan bellows was attached to a rocking bed so as to give him positive pressure when the feet were descending. The respiratory tract infection produced Pseudomonas aeruginosa on culture. The tracheobronchial secretions slowly diminished over a period of two weeks when 20 mg. of polymyxin was administered by aerosolization three times daily. This permitted closing the tracheostomy tube for long periods of time and finally removing it. Since then he has breathed much more easily and has required only a chest respirator or rocking bed, though the vital capacity remains 0.6 liter.

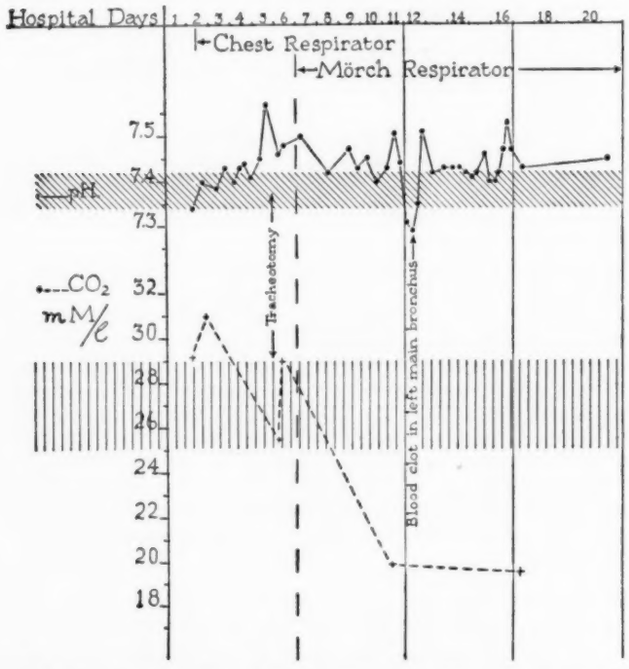

Fig. 4.—pH and volume of carbon dioxide in venous blood of patient in case 2 during artificial respiration. Mild respiratory alkalosis maintained.

Respiratory Equipment

The following devices have been tried and found satisfactory for artificial respiration by intermittent positive-pressure breathing through an uncuffed tube.

Monaghan (Diaphragm) Postive-Pressure Attachment.—The Monaghan positive-pressure attachment consists of a metal housing divided by a diaphragm. The air from the Monaghan respirator moves the diaphragm up and down, forcing humidified and/or oxygenated air from the other side of the diaphragm into the patient. The stroke volume is indicated on a scale attached to the diaphragm and can be increased to 1.5 liters. Also, the pressure can be regulated.

Emerson Hand Bellows.—The Emerson hand bellows is a simple, portable device suitable for short-term use during transportation of the patient or during x-ray examination. The bellows are hung on the belt of the operator, so that the bellows can be pumped with one hand while the other holds the connection to the patient's tracheostomy or face mask.

Huxley Positive-Pressure Valve.—The Huxley positive-pressure valve is used in connection with the Huxley piston-type respirator. The pressure administered is indicated and controllable. Three limitations of this valve are that it sticks when humidity is used, it will operate only in the vertical position, and there is a large dead space in the tubing.

Bennett Self-Cycling Respirator.—The Bennett self-cycling respirator is the only "blower" type of machine that we have been able to adapt for intermittent positive-pressure breathing via the uncuffed tracheostomy tube. Pressure is indicated and can be controlled. Humidity can be administered.

Mörch Respirator.—The Mörch respirator consists of a motor-driven piston pump that drives air through a valve into the trachea. This valve allows the patient to exhale to the room while fresh air is sucked into the cylinder. The stroke volume can be increased to 4 liters but is commonly adjusted to about 0.5 to 1.5 liters. The air can be humidified and mixed with oxygen.

Tracheostomy

For tracheostomy an ordinary Chevalier Jackson silver tracheostomy tube is used without inflatable cuff. It is often a problem to adapt the positive-pressure device to the tracheostomy tube. We have used two methods that do not reduce airway diameter. 1. A rubber baby-bottle cap has proved effective. The inner cannula is pushed through a hole cut in the center of the cap. The part that usually slips over the bottle slips over the pressure tubing. This system originated in the department of pediatrics at Ann Arbor, Mich., and has been described elsewhere.[6] 2. A flange may be soldered onto the inner cannula of the tracheostomy tube. This permits the adaptation of positive-pressure equipment directly without encroaching on the inner diameter of the system. Such tubes are commercially available.

Tube Size.—The larger the tracheostomy tube, the more likely it is that air will enter the lungs in preference to leaving through the nose and mouth during the positive-pressure phase of respiration (fig. 2). A certain amount of air will always "leak" up through the larynx, but this is desirable as a safety device against excessive pressure in the lungs and will blow secretions in the pharynx up toward the mouth. In the acute phase of disease, when tracheobronchial secretions are profuse, large tracheostomy tubes are necessary; e. g., sizes 6-8. However, as secretions decrease, smaller tubes have proved practical. The tube must be big enough to accommodate easily an effective suction catheter.

Valves.—An expiratory valve is usually used in the tubing between the respirator and the patient in order to permit air to leave the patient's lungs via the tracheos-

6. Gish, G.: Connection of Tracheotomy Tubes, Am. A. Inhalation Therapists Bull. 8: 1, 1955.

tomy tube while the respirator is filling with fresh air. Such a valve is usually of the pressure-balanced type resembling an inflatable rubber mushroom. However, one of us (E. T. M.) has developed a simple plastic float valve that does not stick in the presence of detergent aerosols as the pressure-balanced type does.

Humidity.—When positive-pressure breathing through the tracheostomy tube is being used as a means of artificial respiration, humidity is essential because the normal air-conditioning process in the nose is bypassed. Most commercially available humidifiers are inadequate. The Hi-Flow nebulizer proved satisfactory in two cases. In some cases distilled water is sufficient for the aerosol. In other cases, bronchial secretions may be viscid and large mucous plugs life-threatening. In such cases, diluted Alevaire was used as a detergent and found to be quite effective in preventing these difficulties.

Adequacy of Ventilation.—The rib cage must move. If no respiratory excursions are observed, then there is ventilatory insufficiency and the cause must be located. The most common cause of failure is secretions, either in liquid form or as a "plug." They may be heard easily at the expiratory valve between the positive-pressure device and the tracheostomy tube and must be removed by suction. Also, in contrast to patients in the tank respirator, it is easy to palpate, percuss, and listen to the chest. If the patient talks a great deal, during which time the vocal cords are drawn apart, much of the positive pressure may be wasted and too little air enters the lungs. The stroke volume of the respirator must be increased to compensate for this leak. It is unnecessary for the patient to make any conscious efforts to close the glottis for intermittent positive-pressure breathing to be effective via the uncuffed tube. It works as well when the patient is asleep as when he is conscious. Cyanosis should never be allowed, because it is usually a sign of grossly inadequate ventilation, though it may be caused by impaired intrapulmonary function.

The total carbon dioxide content and pH of venous blood can now be determined in many hospitals and should be kept at about normal levels, if the serum sodium and chloride are known to be normal. A mild respiratory alkalosis induced passively is without danger; in fact, it is desirable in the acute phase of poliomyelitis. In the convalescent phase of poliomyelitis slight respiratory acidosis is justifiable because it helps in "weaning" the patient from the respiratory equipment. Alveolar air and arterial blood have been analyzed for gas tensions in a few patients. If such research techniques are available, they can be of immediate clinical value.

Comment

In comparison with the tank respirator the following advantages of this system have been noted: 1. The patient can be examined easily, especially his chest, and the blood pressures can be checked more easily. 2. Medical and nursing care are facilitated. Intravenous infusions and catheterization of the urinary bladder can be carried out more easily; the patient may be turned from side to side or prone, and better skin care can be achieved. 3. Physical therapy is facilitated because the patient is more accessible and greater range of motion is possible. 4. Equipment is smaller and more easily managed by untrained personnel than is the tank respirator. 5. This system is less likely to produce gastric dilatation. 6. Sedatives and narcotics may be given.

The chief disadvantage is the necessity of a tracheostomy. The hazards and complications of tracheostomy are such as to deter one from performing the operation solely to permit ventilation by intermittent positive-pressure breathing via the tracheostomy tube. However, when a tracheostomy is required in a patient with respiratory paralysis, this would seem to be the logical system to use for artificial respiration in order to eliminate the tank respirator. A second disadvantage of this system is the possibility that the tubing from the respirator to the patient may disconnect itself. This is analogous to the possibility for leaks to develop in the tank respirator. Such accidents can be prevented by the proper mechanical safeguards. An alarm that rings when pressure is not developed intermittently in the tubing to the patient has been used to warn the nursing staff of such accidental disconnections.

Summary and Conclusions

In an effort to determine the proper place of intermittent positive-pressure breathing through the uncuffed tracheostomy tube, various respiratory devices were tried. One was designed and built in a university laboratory; the rest are commercially available. From the point of view of respiratory physiology, there is no significant difference between breathing by intermittent positive-pressure at the upper airway and intermittent negative-pressure around the body.[7] No circulatory complications have been observed. Thus, it would seem logical to make use of the greater facility for patient management given by intermittent positive-pressure breathing via the uncuffed tracheostomy tube when artificial respiration is needed in a patient with a tracheostomy.

950 E. 59th St. (37) (Dr. Mörch).

7. Whittenberger, J. L.: Medical Progress: Resuscitation and Other Uses of Artificial Respiration: Part 1, New England J. Med. **251**: 775, 1954; Part 2, ibid. **251**: 816, 1954.

Liver Disease.—The most important features in the treatment of liver disease are rest and the successful administration of a high protein, high caloric diet. In acute infectious hepatitis, bed-rest with bathroom privileges should be observed at least until there is evidence of diminishing bilirubinemia, and preferably until the one minute serum bilirubin is 1.0 mg. % or less. In chronic liver disease, similar bed-rest probably should be continued as long as the patient is showing evidence of improvement. While adequate caloric intake alone will provide improvement in liver disease, the most striking improvement in chronic liver disease results from a high protein intake over a period of many months to combat the serious nitrogen depletion. Alcohol should be omitted entirely. Vitamins, lipotropic agents, testosterone and adrenal hormones offer no additional advantage in average cases of liver disease. The complication of ascites can be managed best by strict sodium restriction in addition to the basic treatment program. The clinician should be alert to the earliest signs of impending hepatic coma: mental disturbance and characteristic tremor. Protein should be administered with caution in such instances, and corticotropin and cortisone may be beneficial. Massive hemorrhage from varices of the upper gastrointestinal tract deserves definitive surgical therapy in most instances to ward off subsequent fatal hemorrhage.—I. F. Tullis, M.D., What Is Important in the Treatment of Liver Disease, *Annals of Internal Medicine*, January, 1956.

CLINICAL NOTES

PNEUMOPERITONEUM AS A DIAGNOSTIC-THERAPEUTIC TEST

TEST TO DETERMINE THE RELATIONSHIP OF ESOPHAGEAL HIATUS HERNIA TO ANGINA PECTORIS

Bernard Maisel, M.D.
and
Eugene Horger, M.D., New York

During the past two decades the similarity of angina produced by coronary arterial insufficiency and that produced by esophageal hiatus hernia has become generally recognized. Von Bergmann,[1] in 1932, was among the first to point out this similarity. In 1933, Harrington [2] reported 60 cases of hiatus hernia in which patients were treated surgically and pointed out the frequency with which the anginal syndrome occurred in them. By 1940 he [3] had collected 198 cases of hiatus hernia and found many had been followed for years with the mistaken diagnosis of coronary arterial insufficiency.

Jones,[4] in 1941, also pointed out the frequency with which the symptoms in patients suffering with hiatus hernia simulated organic heart disease. He indicated that the severity of the symptomatology was not necessarily related to the size of the hiatus hernias; small hernias could cause severe angina, and large hernias could exist without signs or symptoms. He found that glyceryl trinitrate (nitroglycerin) afforded relief from the angina of hiatus hernia. In 1942, Gilbert [5] suggested that the hiatus hernia might aggravate the coronary insufficiency by producing some degree of reflex spasm of the coronary arteries. He believed that careful medical management of the patient would relieve the angina pectoris. Clark [6] also pointed out the possibility that hiatus hernia might aggravate cardiovascular disease. That the loss of blood to the alimentary tract due to the hernia and the resulting secondary anemia might be a causative factor in producing the pain of coronary insufficiency was suggested by Ernstene and McGurl.[7]

Nuzum [8] made a study of 100 patients with angina pectoris, and, although there was no reason to suspect gastrointestinal tract disease in them, a careful search for an esophageal hiatus hernia was made. Twenty-five patients in this group were found to have an esophageal hiatus hernia. He, like Jones, found that glyceryl trinitrate relieved the angina in this group. He also found that the degree of symptomatology was not necessarily related to the size of the hiatus hernia. This study again pointed up the fact that esophageal hiatus hernia and heart disease may coexist and that the specific etiology of the pain might well be difficult to establish. Beckh and Huffman,[9] too, noted that the size and type of hernia was of little or no importance and that the symptomatology often varied inversely to the extent of the herniation.

VanDellen [10] reported a case of a patient with a normal electrocardiogram and heart function when the esophageal hiatus hernia was reduced and a typical coronary insufficiency pattern when the gastroesophageal herniation occurred. Gilbert, LeRoy, and Fenn [11] found that the distention of abdominal viscera caused typical spasm of the coronary artery. Master [12] and co-workers felt that the two-step exercise test and the anoxia test might well help in the differential diagnosis of angina of coronary arterial disease and angina due to esophageal hiatus hernia. They felt that, with few exceptions, a hiatus hernia fails to produce typical anginal pain on effort unless there is underlying coronary artery disease.

Inasmuch as an esophageal hiatus hernia may produce angina in an individual who has coronary arterial insufficiency, the differential diagnosis is often difficult or impossible to establish. In spite of the use of an exercise tolerance test, the differentiation of the etiology of pain is not always possible. It is thus apparent that other diagnostic methods are needed to aid in the diagnosis of such cases. If the angina in a particular case was due to a hiatus hernia, the hernia should be repaired. However, an individual with manifest electrocardiographic and clinical evidence of coronary artery insufficiency as the cause of the pain should not be subjected to anesthesia and an operation. During the past three years we have been interested in the diagnostic and therapeutic value of pneumoperitoneum in esophageal hiatus hernia,[13] and from among the cases studied we believe that it may be of value to report in detail the case of a particular patient because of his long history, the difficulty in differential diagnosis, the value of pneumoperitoneum in establishing the etiology of the disabling pain, and the success of the ultimate hernioplasty in relieving the patient of his angina.

Report of a Case

A 60-year-old male saladmaker was first seen at the New York Hospital, June 21, 1949, because of severe angina. In 1945, the patient had first noted intermittent attacks of precordial and substernal pain that often radiated to the left shoulder and at times extended to the left hand. These attacks were precipitated by excitement, anxiety, and exertion. Initially the pain lasted only a few minutes and would spontaneously disappear. His private physician advised him to "take it easy" and gave him phenobarbital to calm his "nerves." By 1949 these attacks of angina were occurring each day and often several times a day

From the Department of Surgery and Department of Medicine, New York Hospital–Cornell University Medical Center.

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11. Gilbert, N. C.; LeRoy, G. V., and Fenn, G. K.: Effect of Distention of Abdominal Viscera on Blood Flow in Circumflex Branch of Left Coronary Artery of Dog, Am. Heart J. **20**: 519, 1940.
12. Master, A. M.; Dack, S.; Stone, J., and Grishman, A.: Differential Diagnosis of Hiatus Hernia and Coronary Artery Disease, Arch. Surg. **58**: 428 (April) 1949.
13. Maisel, B., and Horger, E.: To be published.

and were precipitated by walking a city block or climbing one flight of stairs. There was no dyspnea, palpitation, orthopnea, cyanosis, or ankle edema.

On physical examination he appeared to be a tense, apprehensive man in moderate distress. The blood pressure was 140/90 mm. Hg. The heart was not enlarged to percussion, and there were no murmurs present. The lungs were clear. The electrocardiogram taken at this time did not differ essentially from one taken four years later (fig. 1). In this electrocardio-

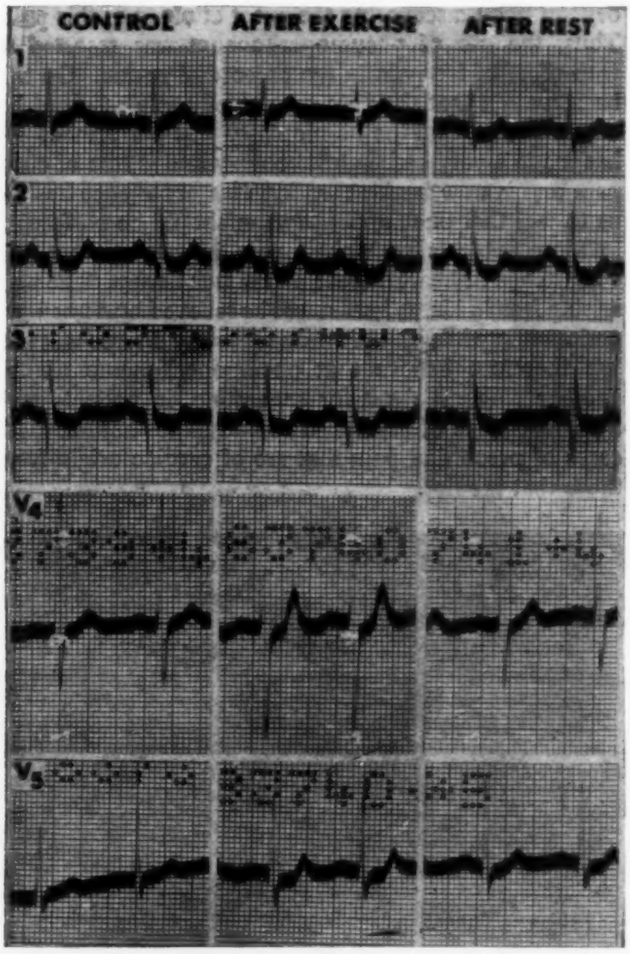

Fig. 1.—Electrocardiogram taken Aug. 24, 1953, during exercise tolerance test before pneumoperitoneum and derived from the three standard leads and chest leads V_4 and V_5. Depression of RS-T segments in leads 2, 3, V_4, and V_5 immediately after exercise fulfilled criteria for positive test. On resting, usual contours of these segments were restored. In figures 1, 3, and 4, standardization in all leads was such that 1 mv. produced 1 cm. deflection of string. Divisions of ordinates equal 10-4 volt and divisions of abscissas equal 0.04 second.

gram the presence of the Q_3 of increased amplitude suggested that a posterior-base myocardial infarction may have occurred in the past. The chest x-ray disclosed the heart size to be at the upper limits of normal. He was treated with whisky, 30 cc. twice daily, and aminophylline, 0.2 gm. three times a day, and on this regimen seemed improved. Occasionally during the next three months he complained of epigastric distress. A gallbladder visualization showed no stones and good function after a fatty meal.

Late in 1949 he was admitted to another hospital because of severe angina. After two weeks of bed rest he was discharged with a diagnosis of "anginal syndrome, no acute EKG changes." Glyceryl trinitrate tablets were added to the regimen of aminophylline and whisky. He soon found that he was taking 3 to 7 glyceryl trinitrate tablets each day, was only able to do light work, and "soon lost his job as a saladmaker." Early in 1950 he was again hospitalized for three weeks at another hospital because of recurrent attacks of severe, crushing precordial pain. A chest x-ray for heart size, with barium in the esophagus, disclosed for the first time a large hiatus hernia.

He was admitted to the New York Hospital, Nov. 6, 1950, for further evaluation. Physical examination again disclosed a tense, apprehensive man in no apparent respiratory distress. Examination of the lung fields was unremarkable. The heart was not enlarged. The sounds were of good quality. A loud, systolic murmur was audible at the apex and transmitted over the entire precordium. Several stool examinations were found to be guaiac-negative. A barium swallow demonstrated (fig. 2*A*) a moderate-sized sliding esophageal hiatus hernia. There was no evidence of ulceration of the mucosa. An exercise tolerance test was performed, and a positive test was obtained. The pattern of electrocardiographic changes during the test were of the same order and magnitude as those that occurred in the exercise tolerance test performed three years later (fig. 1) just prior to the pneumoperitoneum. Esophagoscopy showed no significant dilatation of the esophagus. The stomach was entered at 36 cm. from the upper incisors. No mucosal abnormalities were noted.

On Nov. 21, 1950, a left phrenic crush was performed under local anesthesia through a cervical incision. Postoperative fluoroscopy demonstrated paradoxical motion in the left leaf of the diaphragm. The patient was well for several weeks, and then the symptoms of angina recurred, which were again relieved by glyceryl trinitrate pills. In addition to the angina, the patient developed severe dysphagia. He said that "food sticks in my chest." To the therapeutic regimen for the angina was now added a regimen for peptic ulcer that included a six-feeding soft diet, tincture of belladonna, an aluminum hydroxide preparation (Amphojel), and phenobarbital. On this regimen the patient had infrequent attacks of angina and epigastric distress and seemed well for a period of approximately three years.

On Aug. 21, 1953, he was readmitted to the New York Hospital because of severe angina of several months' duration that occurred after the slightest exertion, after emotional upset, or after eating. A physical examination was unchanged from that of his previous admission of November, 1952. The exercise tolerance test was repeated on Aug. 24, 1953, and again found to be positive (fig. 1). The diagnosis was still arteriosclerotic hypertensive cardiovascular disease, with coronary insufficiency and hiatus hernia. On Aug. 26, 1953, a pneumoperitoneum was begun with 1,000 cc. of air. Within two days there was considerable relief of angina and the epigastric distress. He was discharged from the hospital and, when seen one week later, continued to be completely relieved of his angina and his epigastric distress. Because a right inguinal hernia was noted, the pneumoperitoneum was discontinued after two weeks. Shortly thereafter his anginal and gastric symptoms recurred, in spite of a strict medical regimen that included glyceryl trinitrate, aluminum hydroxide, six-feeding diet, phenobarbital, and methantheline (Banthine) bromide, and he was soon taking 4 to 7 glyceryl trinitrate tablets per day.

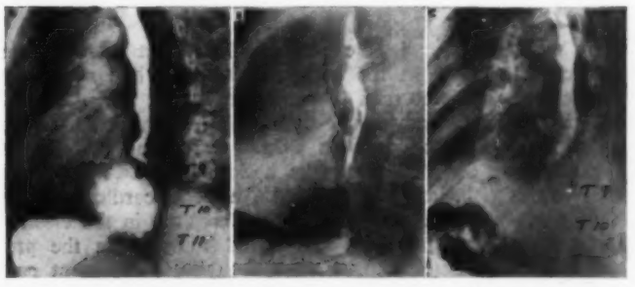

Fig. 2.—*A*, left posterior oblique roentgenogram of the barium-filled esophagus and stomach revealed large "sliding type" esophageal hiatus hernia. *B*, after pneumoperitoneum had been induced, left lateral roentgenogram of the barium-filled esophagus and stomach taken with the patient standing revealed hernia sac filled with air. Stomach lies entirely below diaphragm. *C*, eight weeks after transthoracic repair of esophageal hiatus hernia using the method of Allison. Left posterior oblique roentgenogram of the barium-filled esophagus and stomach revealed normal esophagus. Stomach lies below diaphragm.

The pneumoperitoneum was reinstituted Nov. 2, 1953, with 500 cc. of air. Refills of approximately 1,000 cc. were administered each week (fig. 2*B*). He became completely free of symptoms from Nov. 2, 1953, until the date of his admission to the New York Hospital on Jan. 1, 1954, for further evaluation and possibly for repair of the hiatus hernia. During the

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eight weeks prior to this admission he had stopped use of all medication and took only an occasional glyceryl trinitrate tablet. His angina and epigastric distress had practically disappeared, and his food no longer seemed to "stick in the middle of his chest." A control electrocardiogram taken Jan. 5, 1954 (fig. 3),

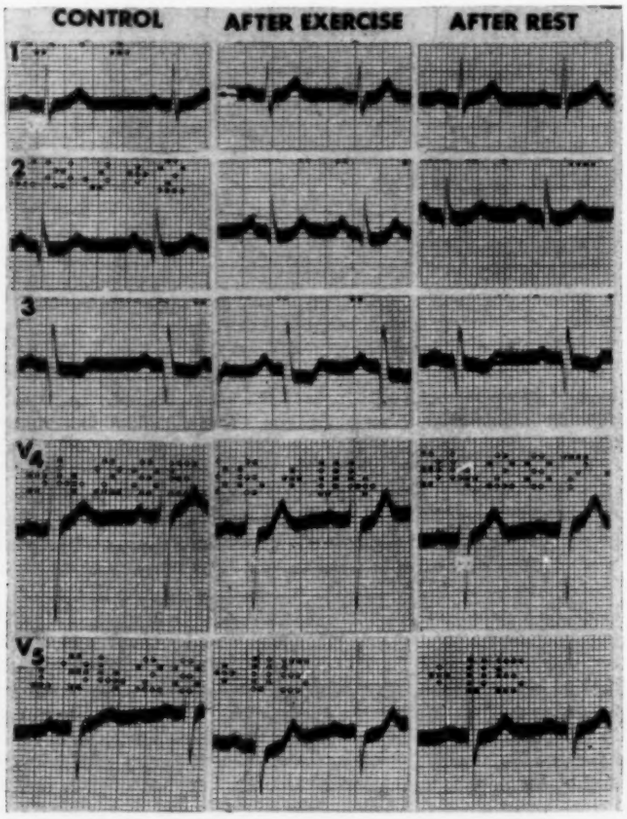

Fig. 3.—Electrocardiograms taken during exercise tolerance test on Jan. 5, 1954, after pneumoperitoneum for five months.

remained unchanged as compared with those taken earlier (fig. 1). The exercise tolerance test, however, was again positive. On Jan. 8, 1954, the hiatus hernia was repaired, using the method of Allison. An x-ray on Jan. 25, 1954 (fig. 2*C*), showed the satisfactory repair of the hiatus hernia. He was discharged on Jan. 16, 1954, without complaint. He was readmitted to the New York Hospital on Feb. 15, 1954, feeling quite well; a right inguinal hernioplasty was carried out. He was discharged on Feb. 22, 1954.

He was next seen in the cardiac clinic eight months later on Oct. 24, 1954. In the interval period he had moved to another state and returned to work five days a week. He had had chest pain on only two occasions during this eight-month period and on both occasions pain was relieved by glyceryl trinitrate. He felt better than he had for years. One month prior to this visit, he had remarried. An electrocardiogram was taken (fig. 4), which revealed for the first time in the electrocardiogram at rest negative and coved T waves in the precordial leads. These changes were thought to represent progression of coronary artery disease. After exercise there were alterations in the RS-T segments in leads 2, 3, V_5, and V_6, indicating a positive test. After 15 minutes the electrocardiogram had not yet returned to its original contour. He experienced no pain with the exercise.

Comment

Since the interpretation of pain in the precordial region is often difficult, particularly in cases with objective findings of coronary disease and an associated hiatus hernia, measures that would aid in the interpretation of the origin of this pain are of value. The case presented clearly points up this problem. This man had precordial pain, and the diagnostic work-up revealed evidence of heart disease as demonstrated by a positive Master's exercise tolerance test. However, the coexistence of a hiatus hernia was also established after the gastrointestinal x-ray study. Was his pain primarily due to his heart disease or was it the result of the hernia? The patient had become practically invalided by his pain, and it was apparent that further successful treatment would depend upon discovering the exact etiology of this pain. Thus, the use of pneumoperitoneum was resorted to with relief of his pain in the precordial region. On this basis we felt that the pain rose chiefly as a result of his hiatus hernia, and the hernioplasty was performed. He has made a very successful recovery and is free of chest pain and is now back at work. This experience has led us to feel that pneumoperitoneum should be performed in more subjects with chest pain in whom there is a coexistence of heart disease and hiatus hernia. The pain arising from a hiatus hernia will be relieved by a pneumoperitoneum while that of coronary artery disease will not. We therefore believe that pneumoperitoneum affords another diagnostic test for separating, in patients with the coexistence of heart disease and hiatus hernia, those cases of precordial pain that are of cardiac origin from those that are not.

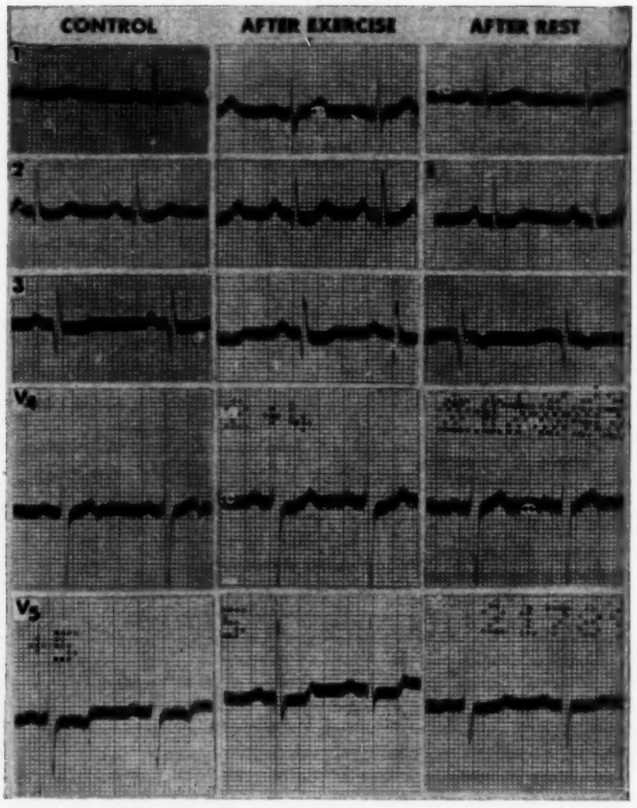

Fig. 4.—Electrocardiograms taken during exercise tolerance test Oct. 25, 1954, eight months after surgical repair of the diaphragmatic hernia.

Summary

A review of the literature pointed out the similarity of angina produced by coronary artery disease and that produced by esophageal hiatus hernia and the difficulty in differential diagnosis. In a patient with coexisting hiatus hernia and coronary heart disease, the use of

pneumoperitoneum aided in the interpretation of the etiology of pain and a successful hernioplasty brought relief of the pain. We feel that pneumoperitoneum affords a means of separating those cases in which the chest pain is caused by an esophageal hiatus hernia from those in which angina is of cardiac origin, where the two problems coexist.

1 E. 69th St. (21) (Dr. Maisel).

AORTIC ANEURYSM AND ANEURYSMAL ENDARTERITIS AFTER RESECTION FOR COARCTATION

REPORT OF A CASE TREATED BY RESECTION AND GRAFTING

William J. Martin, M.D.
John W. Kirklin, M.D.
and
James W. DuShane, M.D., Rochester, Minn.

Three cases in which aneurysm of the aorta developed at or near the site of anastomosis after resection for coarctation have been reported,[1] but there is no record of a case such as this one, in which the condition was complicated by intra-aneurysmal endarteritis.

A 6-year-old boy had undergone surgical correction of coarctation of the aorta on April 21, 1953, 10 months before we saw him. The aorta had been clamped near the origin of the intercostal artery that was uppermost in the operative field, and near the base of the subclavian artery. Then a segment of the aorta 1 cm. in length had been resected. The incision across the proximal part of the aorta (the part between the aneurysm and the heart) was described as oblique, so that the lumen of each cut end of the aorta had been about 2 cm. in diameter. End-to-end anastomosis had been made, with use of a continuous, everting mattress suture, interrupted four times, with single mattress sutures at each interruption.

The pulsations in the lower extremities had been vigorous immediately after operation, but the blood pressure in the upper extremities had remained at preoperative levels. The boy had been dismissed from the hospital 10 days after operation. He then had complained of severe abdominal cramping and had been returned to the hospital. The blood pressure at that time, presumably in the arms, varied from 180 to 200 mm. Hg systolic and 100 to 110 mm. Hg diastolic. Two days after his second admission the boy had been dismissed. That evening he had passed bloody urine and had been admitted to the hospital for the third time. Thereafter urine had been scanty and coffee-colored; then the patient had been anuric for 36 hours. He had been dismissed from the hospital 10 days after his third admission.

In the latter part of June, 1953, the boy had complained of pains in his legs and inability to walk. Petechiae had appeared on the legs and soles of the feet, and the boy's temperature had ranged from 101 to 103 F (38.3 to 39.4 C). Roentgenograms had given evidence of the presence, at the approximate level of the aortic anastomosis, of a mass that had been interpreted as a pseudoaneurysm. In early July, 1953, the generalized abdominal cramping pains had recurred. In September, 1953, the boy had begun to complain of severe headaches and of a burning pain on the dorsum of his right foot. The area on the right foot of which complaint was made subsequently had become swollen, red, and exquisitely tender. On several occasions the feet and legs had been affected as the right foot had been, usually after an episode of chills and fever. On Thanksgiving Day (November) 1953, the upper part of the left arm had been similarly affected. In early January, 1954, there had been an episode of chills, fever (temperature 104 F [40 C]), gross hematuria, and severe abdominal pains.

On Feb. 21, 1954, when the boy was admitted to the Mayo Clinic, he was pale, slender, weighed 42 lb. (19 kg.), and appeared chronically ill. The oral temperature was 98 F (36.6 C). Blood pressures in the right arm were 124 mm. Hg systolic and 78 mm. Hg diastolic; in the left arm corresponding pressures were 126 and 80 mm. Hg. In the left leg the blood pressure was 122 mm. Hg systolic and 94 mm. Hg diastolic, but evidence of blood pressure in the right leg could not be obtained after repeated efforts. A soft systolic murmur, grade 1, could be heard best over the first and second left intercostal spaces. The second aortic sound was of moderately increased intensity and split. A systolic bruit, grade 2, was heard in the upper part of the left scapular region. It was presumed that there was a false aneurysm of the aorta at the site of the anastomosis and that recurrent emboli, originating in lesions of subacute bacterial endarteritis, also of the region of the anastomosis, had been swept in the blood stream to the extremities.

Fig. 1.—Roentgenogram of thorax before operation.

On admission, results of laboratory examinations were as follows: The urine was normal. The concentration of hemoglobin was 11 gm. per 100 cc. of blood. Erythrocytes numbered 3,730,000 and leukocytes 14,800 per cubic millimeter of blood. Of the leukocytes, 13% were lymphocytes, 1% monocytes, 71% segmented neutrophils, and 15% band neutrophils. The sedimentation rate of erythrocytes was 31 mm. per hour (Westergren method). The value for blood urea was 34 mg. per 100 cc. In roentgenograms (fig. 1) there was a rounded shadow in the left side of the superior mediastinum, a surgical defect in the posterior portions of the fifth and sixth left ribs, and a shadow of calcific density, overlying the area of the left kidney, measuring 3 by 5 mm. and consistent with renal lithiasis. On fluoroscopy there appeared the shadow of a pulsatile, well-circumscribed mass that could not be separated from the aorta. Tomograms of the thorax demonstrated that the mass involved the posterior portion of the aortic arch as it turned into the descending aorta.

On excretory urography, the pelvis of the right kidney and the right ureter appeared normal, the calices seemed minimally blunted, and there were suggestions of some inflammatory

From the Section of Medicine (Dr. Martin), the Section of Surgery (Dr. Kirklin), and the Section of Pediatrics (Dr. DuShane), the Mayo Clinic and Mayo Foundation.

The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

1. (*a*) Crafoord, C.; Ejrup, B., and Gladnikoff, H.: Coarctation of the Aorta, Thorax **2**: 121-138 (Sept.) 1947. (*b*) Blickman, J. R.: A Case of Aneurysm of the Aorta After Resection for Co-Arctation (Cured by Excision), Arch. chir. neerl. **1**: 50-56, 1949. (*c*) Ducuing, J.; Enjalbert, A.; Eschapasse, H., and Moreau, G.: Les suites d'une greffe d'aorte humaine conservée pour rétrécissement de l'isthme de l'aorte, Mém. Acad. chir. **80**: 406-414 (March 24-April 7) 1954.

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changes; the left renal pelvis and the upper and lower calices appeared normal, but the middle calices seemed somewhat scarred and distorted. The previously mentioned calcific shadow on the left appeared to be included in a minor calix. These findings suggested bilateral chronic pyelonephritis and a left renal calculus. On cystoscopy, under anesthesia with thiopental sodium, mild chronic inflammation of the trigone and scattered

Fig. 2.—Aneurysm as seen at operation. Vessel immediately above the aneurysm is left subclavian artery. Umbilical tape is around the aortic arch between left subclavian artery and left common carotid artery, but this portion of arch is not visible. Further dissection was necessary in order to visualize it.

lesions of cystitis cystica were seen. A retrograde cystogram gave evidence only of a normal state. Cultures of the urine gave negative results.

In order to isolate the micro-organism that, it seemed likely, was infecting the blood stream, use of the antibiotics that the boy had been taking at home was discontinued. For five days after his admission to the hospital the boy had no fever, but on the sixth day, late in the evening, his temperature suddenly rose to 105 F (40.5 C). This fever was accompanied by chills and slight perspiration. For the ensuing three days there was again no abnormality of temperature, but, from the 10th day of hospitalization onward, there were daily elevations of temperature, generally late in the evening, ranging from 101 to 105 F. Blood cultures were made daily from the time of admission, but were consistently negative after two days of growth. However, in blood drawn on Feb. 26, 1954, after 12 days of culture, there was found a gram-negative filamentous organism that grew in liquid medium only. This organism was tentatively classified as a member of the genus Alcaligenes. Subsequent cultures of the blood gave negative results until that drawn on April 9, 1954, from which an organism identical with that obtained on Feb. 26, 1954, was grown. So-called sensitivity tests demonstrated that the organism resisted a preparation of streptomycin in amounts greater than 25 mcg. per milliliter and was sensitive to the tetracycline group of antibiotics in amounts of 3.1 mcg. per milliliter.

Because of the strong clinical impression that the boy had subacute bacterial endarteritis, we decided to use antibiotics. We were aware that a bacillus difficult to type, which grew out only after 12 days, and which could be grown only in liquid medium, was an unusual cause for bacterial endarteritis. However, the bacteriological data did agree with the knowledge of the child's failure to respond to prolonged treatment with penicillin and with the inability to demonstrate a causative organism in previous bacteriological studies. Accordingly, 250 mg. of oxytetracycline hydrochloride was given by mouth every six hours, and 250 mg. of dihydrostreptomycin sulfate by intramuscular injection twice daily for a week before operation. The temperature was normal after four days of antibiotic therapy and remained normal until the time of surgical operation, three days later.

When the thorax was opened on April 19, 1954, a pulsating false aneurysm, about 10 cm. in diameter, appeared to have dissected its way partly into the fissure between the upper and lower lobes of the left lung (fig. 2). The left subclavian artery, the aortic arch between the left subclavian and left common carotid arteries, and the descending aorta distal to the aneurysm were isolated. The aneurysm was mobilized posteriorly and to the left, but four pairs of intercostal arteries had to be cut. Further dissection allowed identification of the thoracic duct and the esophagus and separation of the lung from the huge pulsating aneurysm without damage to either. The aneurysmal wall was dissected away from the transverse portion of the arch down toward the region of the anastomosis and ultimately to a point just distal to the take-off of the left subclavian artery. One clamp was placed across the aorta just proximal to the aneurysm. Another clamp closed the aorta distal to the aneurysm. The aorta was then transected just distal to the proximal clamp. After the aorta had been peeled up out of its bed the small communicating branches were ligated. The aorta was then transected just distal to the aneurysm to complete the resection. A preserved, homoiogous aortagraft of proper size was inserted and fixed in place with interrupted, everting mattress sutures (fig. 3). There was excellent pulsation in the descending aorta after the operation, although prior to it the descending aorta was not pulsating significantly. Use of oxytetracycline hydrochloride and dihydrostreptomycin sulfate in the amounts stated above was continued for a week after operation. The only rise in temperature in the postoperative period was to 101 F (rectally) on the evening of the operation.

The boy was dismissed from the hospital on the ninth postoperative day after an uneventful convalescence. Just before his leaving for home, the blood pressures in the right arm were 125 mm. Hg systolic and 80 mm. Hg diastolic; the corresponding pressures in the left arm were 130 and 85. In the thorax, murmurs or bruits were not heard, but breath sounds over the left anterior aspect were slightly suppressed. Pulsations in the left femoral artery now were adequate. In the right femoral

Fig. 3.—After resection of aneurysm and its replacement with a preserved homologous aortic graft. Again the left subclavian artery is visible, and now the aortic arch between the left subclavian artery and the left common carotid artery is clearly shown.

artery, the vessel in which no blood pressure had been registered on the boy's admission, pulsations were not detected. This finding was thought possibly to be attributable to an old thrombotic occlusion of the right iliac artery. It was suggested that after the boy had returned home urinalyses be repeated at intervals, in view of the probable chronic pyelonephritis, and that definitive treatment be provided if infection was found.

The pathologist reported that the tissue removed at operation contained an aneurysmal enlargement 6 cm. in diameter and that silk suture material, forming a loop 1 cm. in diameter, projected into the lumen of the aneurysm (fig. 4). Subacute bacterial endarteritis apparently had taken origin in the immediate vicinity of the foreign agent, and a resulting thrombus contained many organisms of a filamentous branching variety. Cultures of the material obtained at operation, moreover, yielded a gram-negative, filamentous organism that was tinctorially and culturally identical with an organism that twice had been isolated from the blood stream of the patient.

In a letter dated Jan. 31, 1955, the home pediatrician wrote that the boy had been well and had attended school regularly since his return home after the second operation. At the same time, a urologist wrote that the roentgenographic density in the region of the left kidney was still there but that, except for an episode of gross hematuria in July, 1954, the condition of the urinary tract seems to be under satisfactory control.

Comment

If an aneurysm is associated with coarctation, satisfactory treatment demands complete removal of the aneurysm along with the coarctation. The gap thus created may have to be filled with a graft.[2] Crafoord, Ejrup, and Gladnikoff [1a] reported a case in which, after resection, a false aneurysm resulted, in their opinion from insufficiency of a aortic suture line, and caused the patient's death. Blickman,[1b] of the University of Amsterdam, also has described an aneurysm of the aorta after resection for coarctation. In Blickman's patient a true aneurysm had formed at, or near, the site of anastomosis; the aneurysm was removed and the defect was closed successfully. Through Blickman we have learned of the case described by Ducuing and others,[1c] wherein an aneurysm developed after resection of the coarctation and placement of a graft.

In cases of aortic coarctation in which surgical treatment is not applied, certain complications can be expected. Usually they are not expected to develop after operation. The fact that they did develop in this case after the first operation makes description of them pertinent here. The intima of that part of the aorta that lies distal to the coarctation often undergoes localized, fibrous thickening that causes it to rise as a corrugated patch above the surrounding intima. This is known as a "jet lesion" and is presumed to be caused by a jet of blood from the zone of aortic narrowing [3] striking the aortic wall. Since elastic tissue of the media beneath the jet lesion may be lost, a saccular aneurysm may develop in this zone, or the lesion may serve as the place of origin of a dissecting aneurysm. The lesion might serve, also, as a nidus for bacterial endarteritis.

Some patients with coarctation of the aorta finally die of causes unrelated to the vascular malformation; however, about 60% of those whose coarctation remains uncorrected die before the 40th year of life, and the principal causes of their deaths are congestive heart failure, rupture of the aorta, intravascular bacterial infections, and intracranial lesions.[3]

Bicuspid aortic valves represent a potential site for the development of subacute bacterial endocarditis. The reported incidence of bicuspid aortic valves in cases of aortic coarctation varies from 23.5 to 42.7%.[3] Seventy per cent of patients who have bacterial endocarditis and coarctation have bicuspid aortic valves.[4] Thus, the principal clinical importance of bicuspid valves is that they are more likely sites than normal valves for the development of bacterial infection. Alpha-hemolytic streptococci are the commonest infecting organisms, according to Reifenstein, Levine, and Gross.[4]

Abbott [5] wrote of 13 among 200 cases of coarctation of the aorta in which bacterial endarteritis occurred at the seat of coarctation. She thought that, since the aorta immediately below the stenosis commonly is dilated and atheromatous, and, since the constricted portion is kinked and deformed, there exists a place of lowered resistance against circulating micro-organisms. She described bacterial outgrowths on the eroded intima, usually at or below the stenosis, with destructive inflammatory changes in the subjacent coats of the aorta, sometimes resulting in a so-called mycotic aneurysm. Three of the mycotic aneurysms in this situation reviewed by Abbott had ruptured. She pointed out that the micro-organisms that produce mycotic aneurysms vary, just as

Fig. 4.—Specimen removed at operation. Note the loose thrombus hanging from the suture line, from which organisms were cultured.

do those causative of bacterial endocarditis. She also wrote that the alpha-hemolytic streptococci are probably the commonest causative agents of the endarteritis that may complicate coarctation of the aorta.

Subacute bacterial endocarditis may result in marked aortic insufficiency, cardiac hypertrophy, high pulse pressures, and associated vascular phenomena, whereas the symptoms of isolated aortitis (subacute bacterial endarteritis) resemble those of endocarditis but do not usually include the signs of aortic insufficiency.[4]

Summary

In the case of aneurysm of the aorta here reported, endarteritis within the aneurysm had been manifested by the usual signs of that complication but chiefly by re-

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current embolism. The causative organism of the endarteritis was a gram-negative filamentous rod, tentatively classified as a member of the genus Alcaligenes. Preoperative administration of oxytetracycline hydrochloride combined with dihydrostreptomycin sulfate controlled the manifesations of the endarteritis. The further fact that other complications were eliminated by the second operation emphasizes the soundness of persisting in surgical effort at cure.

AN IMPROVED AND ROTATABLE ANOSCOPE

Daniel J. Abramson, M.D., Washington, D. C.

Anoscopes in current use are usually of two types. The speculum is either beveled at the end or has a longitudinal cutout part for inspection of the anorectal area. Both types have certain disadvantages. With the former, the instrument frequently slips out during the course of the examination and many insertions are necessary before the examination is completed. The difficulties of reinsertions in the obese patient can be readily understood. With the latter type, the cutout portion of the speculum is too narrow for proper evaluation of the anal area, the edges are sharp, and rotation pinches or cuts into the mucosa. In addition, these anoscopes are of solid construction and rotation must be accomplished by motion of the handle.

With these objections in mind, a new anoscope has been designed to provide for the complete examination and evaluation of the anorectal area. This instrument allows distal, intermediate, and proximal vision by means of a distal beveled portion, an intermediate longitudinal

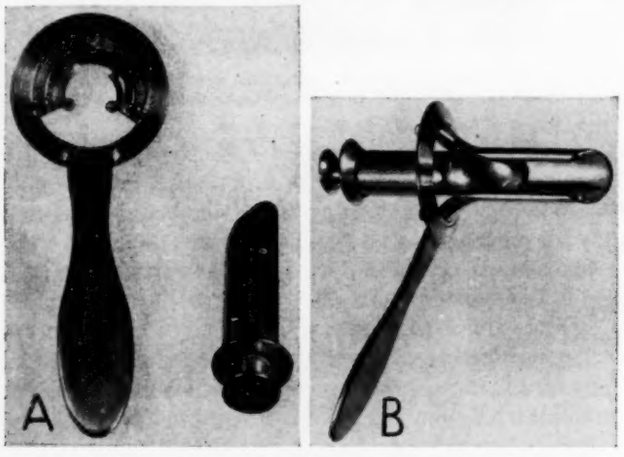

Fig. 1.—*A*, front view of anoscope. Note rolled edges and flanges of speculum. *B*, lateral view of anoscope. Obturator has been partially inserted.

cutout part, and a proximal flared portion. The flared portion permits simultaneous inspection of the anal skin. The edges of the speculum that come in contact with the mucous membrane are rolled to facilitate rotation without pinching. The feature of a rotatable speculum on a stationary, universal handle has been added so that only one insertion is necessary to completely examine the anorectal area. Thus, this anoscope is universally useful in the anal examination, even if the patient is obese.

From the Department of Surgery, Georgetown University Hospital.

The instrument (fig. 1) consists of four parts. The handle, which fits comfortably in the fingers and palm, is combined with a grooved ring-shaped portion adapted for insertion of the speculum. The speculum is tubular and open at both ends. The distal end of the speculum is beveled. The other end is flared for insertion into the handle and to permit visualization of the external anal

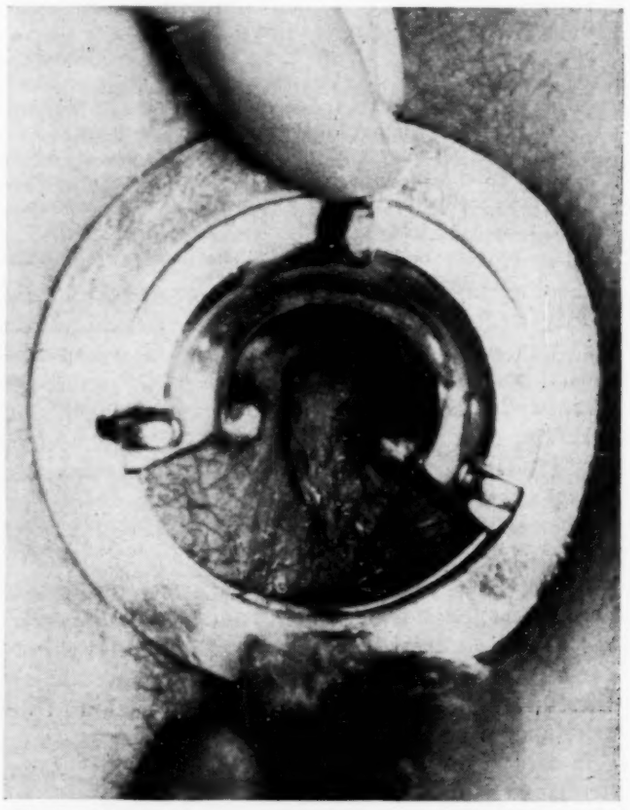

Fig. 2.—Anoscope in place in patient with marked hemorroids. Rolled edges on rotation pass easily over hemorrhoidal tissue without pinching.

area. Three flanges are present on this part to permit easy rotation. The cutout portion of the speculum extends the entire length and is wide enough to permit visualization of one third of the anal circumference. The edges of the slotted portion are rolled so as to avoid pinching the mucosa when the instrument is rotated. The retaining ring is egg-shaped and made of spring steel so that it can be snapped in place, thus locking the speculum in position. The ring can be easily disengaged for cleaning the component parts. The obturator is cylindrical, tapered, and rounded at one end for easy insertion. There is a longitudinal groove on each side designed to fit over the rolled edge of the speculum.

The anoscope is easily inserted into the anus. The obturator is removed and inspection of the anus is accomplished by rotating the flanges of the speculum. In figure 2 the anoscope is seen in place in a subject with marked hemorrhoids. The rolled edges pass smoothly over this redundant tissue. Other features of this instrument are worthy of mention: The speculum can be used without the handle if so desired; the anoscope is easily disassembled for cleansing; it is a useful instrument for the injection treatment of hemorrhoids; various sized speculums can be made for use with the universal handle; lighting features can easily be added; and this type of instrument can be constructed for examining other body cavities.

Summary

A new anoscope not only features a rotatable speculum on a universal stationary handle but also combines and improves upon the features in existing anoscopes. Distal, intermediate, and proximal viewing is permitted. Only one insertion is necessary for the complete evaluation of the anal area, and rotation does not cause pinching, since the edges are rolled. It is believed that this anoscope is the easiest to handle and offers the widest range of vision and therefore is the instrument of choice for the anal examination.

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COUNCIL ON FOODS AND NUTRITION

Statement of the Council

The Council has authorized publication of the following statement concerning "The Safety of Artificial Sweeteners for Use in Foods," a report of the Food Protection Committee, Food and Nutrition Board of the National Research Council.

EUGENE H. STEVENSON, M.S.
Acting Secretary

ARTIFICIAL SWEETENERS

During the decade ending in 1950 many new chemicals were developed for use as functional food additives. The hearings of the Food and Drug Administration for definition and standards of identity of foods emphasized to the public the increasing usage of chemical additives. Public attention was even more strongly directed to the matter when a committee of the House of Representatives (Delaney committee) investigated the use of chemicals in foods.

Prompted by these developments and at the request of a variety of industrial organizations, the National Research Council in 1950 established the Food Protection Committee as a committee of the Food and Nutrition Board. The committee serves as a fact-finding and policy-advisory body for government and industry and deals with public health implications of the use of chemicals in foods. Financial support to the National Research Council from chemical, food, and packaging industries, commercial laboratories, and interested persons provides funds for a secretarial staff and for committee work. Committee members serve without compensation.

The National Research Council has published a number of reports prepared by the committee concerning the use of chemicals in the production and processing of foods. The most recent of these, "The Safety of Artificial Sweeteners for Use in Foods," is of special interest to the medical profession.[1] It reviews available information concerning toxicity of saccharin and the cyclamates, which are widely used sweetening agents.

A great many studies of the biological effects of saccharin have been made. The most extensive of these in man were conducted for the Referee Board of Scientific Advisors to the Secretary of Agriculture in 1911 by Christian Herter and Otto Folin.[2] In these studies, men consumed up to 1.5 gm. of saccharin per day for periods varying from five months for the low intakes to two months for the high intakes. Careful clinical and laboratory examination revealed no significant harmful effects of such intake and in addition showed that saccharin is rapidly excreted unchanged in the urine.

Recent investigations [3] of chronic toxic effects of saccharin in rats have corroborated the findings made in the early years of study of saccharin, that saccharin is relatively nontoxic. An ingestion level of 1% of the diet throughout the life span from weaning had no measurable effect on rats, and a level of 5% of the diet over the life span caused only slight retardation of growth.

The cyclamates (the sodium and calcium salts of cyclohexylsulfamic acid) have been studied extensively since their introduction for use as sweeteners in 1950. Studies in laboratory animals [4] have revealed no significant adverse effects produced by cyclamate at 1% of the diet or less. At 5% of the diet slight toxic effects, mild inanition and moderate diarrhea, are noted. Diarrhea results in rats fed cyclamate at levels of 1 gm. per kilogram of body weight and in dogs fed 2 to 4 gm. per kilogram.

In healthy men the only observed adverse effect of cyclamate has been softening of stools at intakes of 5 gm. or more per day.[5] Studies with laboratory animals indicate that this effect, which is probably caused by the osmotic activity of cyclamate,[4b] seems to be without hazard to health.

This report of the Food Protection Committee concludes, "There is no evidence that use of the nonnutritive sweeteners, saccharin and cyclamates, for special dietary purposes is hazardous." The report emphasizes that knowledge of and experience with the use of cyclamate are more limited than they are with saccharin and that continued study of the material is required before certain questions can be answered. For example, no data exist concerning the minimum laxative dose of cyclamate for children; knowledge of the mechanism of excretion of the sweetener is incomplete, and considerations that may be of importance to its use in pregnancy, lactation, colonic conditions, or instances of renal dysfunction are incompletely known. The report further suggests that continued observation of persons using cyclamate is desirable.

This valuable report gives a reassuring appraisal of the safety of these sweeteners for special dietary purposes but does not support the unrestricted use of these sweeteners in general purpose foods and beverages.

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CHRONIC PROGRESSIVE RESPIRATORY FAILURE

GUEST EDITORIAL

Max S. Sadove, M.D.

The medical student as well as the medical practitioner has a mental concept of circulatory failure. He distinguishes between the central, or cardiac, and peripheral, or shock, type of failure. He is taught how to diagnose the chronic or progressive stages of cardiovascular diseases and learns how to recognize the signs, symptoms, and treatment of various forms of heart failure. In the larger centers, there are actual "heart stations" for diagnosis of the more complicated cardiac diseases. Even the smallest hospitals have equipment that is useful in aiding in the diagnosis of various forms of heart disease. But, with respiratory diseases, equipment for the teaching of diagnosis and therapy is lacking in all but a few large centers.

Respiratory function units are available in only a few places. This would tend to make one think that there is no such entity as respiratory disease or that the cardiac function laboratories can solve the entire problem. (It is admitted that most good cardiac function laboratories can and do make the distinction between primary respiratory or primary circulatory disease.) The diseases referred to the heart station are cardiorespiratory, with dominance in one or the other components, but the chronic, progressive diseases go unchecked because of a lack of a lung station.

As one visualizes the hospitals of the United States, one is impressed with the fact that the heart receives a great deal more attention than the lung. This is as it should be. Almost every hospital has the minimal equipment necessary for the diagnosis of cardiac disease, but, when it comes to respiratory diseases, there is an extreme dearth of diagnostic and therapeutic equipment and respiratory physiologists. In fact, the type and amount of inhalation diagnostic and therapeutic equipment found in hospitals vary with the interest shown by various staff members. Whether this state of affairs is justifiable is questionable. Certainly no real practitioner of medicine would deny that there are large numbers of patients who have chronic bronchitis, asthma, or bronchiectatic, emphysematous, and other similar states. If these are to be treated logically, certain minimal diagnostic and therapeutic equipment must be available. If they are not available, the therapy would be based on a crude clinical guess rather than an accurate diagnosis.

The progressiveness of many of these diseases is not adequately appreciated because of the mildness of their course and also because by various therapeutic procedures they can be halted momentarily. However, diseases that are found in this group (asthma, bronchitis, emphysema, and bronchiectasis) frequently are progressive to the degree that the heart and vessels are affected, or the original disease progresses to the point where these diseases become a major problem.

It is to be hoped that the practitioner in every medium-sized city may be able in the near future to send his patient to a lung station and get back a statement that will be effectual to direct him in his treatment and diagnosis. Without these tests, much of the treatment is rather nonspecific. One should at least know that there is trapping on inspiration or expiration, that there is diminished timed volume, that there has been an improvement or no improvement in such data as minute volume and nitrogen washout, that there has been a change in carbon dioxide level, that the effort of inspiration or expiration is increased, and what the degree and speed are at which each can be accomplished.

At first glance, these data seem extremely complex, but they can be easily interpolated and reported on, so that they could be of value to the average clinician, but these diagnostic tools would be of little value unless adequate associated equipment for therapy were made available. Units for aerosol therapy, instruments for intermittent positive pressure, physical therapy department equipment for muscular exercises, and such measures as abdominal supports are all essential, but, most of all, there is a need for interest on the part of medical personnel in these patients with chronic progressive respiratory diseases. With simple exercise, aerosol therapy, and intermittent positive-pressure therapy, many of the diseases now classed as progressive may be slowed—many respiratory cripples may be returned to a useful life. This would be possible if the tools now available in a few areas were made easily available to more patients.

Professor of Surgery, Division of Anesthesia, University of Illinois College of Medicine, Chicago 12.

POSTINFUSION HYPOGLYCEMIA

Occasionally disturbing but seldom alarming clinical manifestations follow shortly after the completion of an intravenous infusion of dextrose. These consist of weakness, fatigue, sweating, disorientation, hypotension, and, rarely, convulsions. If a blood specimen is examined at the time, the sugar level will be found to be quite low, thus identifying the reaction as due to hypoglycemia. Usually the untoward signs and symptoms disappear spontaneously as the blood sugar level returns to normal, but in any case they can be immediately corrected by a second infusion of dextrose. Even when there is no clinical evidence of hypoglycemia, a fall in blood sugar level

nearly always follows every intravenous infusion of dextrose. It is not known, of course, whether this fall has any occult, deleterious, or other effects.

The existence of this postinfusion hypoglycemia is, of course, well known and indeed is similar to but perhaps more pronounced than the postabsorption hypoglycemia that follows the ingestion of glucose in the common procedure of doing a glucose-tolerance test. The reason for the hypoglycemia is thought to be a persistence into the postabsorptive period of the mechanism by which the load that has led to hyperglycemia is removed from the blood during the absorptive period. This mechanism is explained as follows: The passage of dextrose into the cell involves its phosphorylation plus an increased production of insulin, a metabolic phenomenon that is slow in starting and therefore presumably slow in subsiding; thus dextrose continues to be removed from the blood stream even after the infusion is over, a reactive phenomenon observed in other physiological states.

In a study on the behavior of the hexose fructose, Miller and others [1] at the Lakeside Hospital in Cleveland noted in three instances in human subjects that the blood sugar level did not fall during the postinfusion period when this sugar was used, as it fell with dextrose. This phenomenon was then made the subject of a careful study by Peden and others [2] at the Homer G. Phillips Hospital in St. Louis. Dextrose and fructose were compared (on different days) in the same patients, each thus acting as his own control. In each of 20 such pairs of experiments, the findings were the same. Dextrose infusions, as was to be expected, were always followed by a fall in the blood sugar level to values below the normal or initial fasting reading. The average maximum fall during three postinfusion hours was nearly 20 mg. per 100 cc. below the fasting level. By contrast, the postinfusion levels after fructose infusion did not fall below the fasting level. In one patient, after dextrose, a typical postinfusion reaction including convulsions and hypotension was observed. None followed fructose infusions.

These observations have considerable theoretical as well as practical significance. From the physiological point of view, they confirm other observations showing that the metabolism of fructose differs from that of dextrose in that it probably enters the cell in the free state and thus requires little or no insulin or phosphorylation.[3] But the practical implications are intriguing. How significant is this effect, especially in the postoperative period, a period in which hypoglycemic symptoms may readily occur after the infusion of dextrose and be attributed to causes other than hypoglycemia? But even if few or no clinical manifestations are evident, how innocuous is even transient hypoglycemia? It is known that insulin-induced hypoglycemia represents a "stress" phenomenon; as a stimulus of gastric secretion it has long been used to test the completeness of vagal interruption in the treatment of duodenal ulcer. Further studies are needed of postinfusion hypoglycemia after administration of dextrose, especially in the postoperative state, to determine how often it is responsible for untoward clinical and subclinical phenomena. If these effects are sufficiently important, it would seem from the above-mentioned studies that they could readily be prevented by using fructose.

INFECTIOUS AGENTS IN SEWAGE

Ideas that have been accepted for many years come to be believed as being axiomatic, but every now and then a critical reevaluation of these ideas is called for and may reveal that the ideas are based on conditions that have changed, that they failed to consider important factors, or occasionally that they were never true. The idea that sewage that has undergone primary and secondary treatment in a modern sewage disposal plant may safely be discharged into a river has been subjected to critical scrutiny by Kelly and her co-workers.[1] The old methods of sampling by dipping up several cubic centimeters of sewage had the disadvantage that it missed many organisms prevalent in sewage that can be demonstrated by examining large gauze swabs that have been suspended in the flowing sewage for prolonged periods —usually 24 or 48 hours. Coxsackie and poliomyelitis viruses were found by the swab method but not by the dip method in the effluent from Imhoff tanks having a retention period of two hours, and, although the results were better after the secondary sewage treatment, consisting of passing the sewage through a trickling filter followed by simultaneous sedimentation and chlorination, such treatment was not always effective in destroying the viruses.

The same observers examined sewage for Mycobacterium tuberculosis, and, since cultural methods were unsatisfactory because of the overgrowth of other organisms, they used guinea pig inoculation. Again they found that more reliable results could be obtained by examining exposed swabs and that tubercle bacilli may be present in streams receiving the effluent from sewage treatment plants, even those using secondary settling and chlorination. As an incidental finding, many of the organisms recovered were resistant to isoniazid. In another study Jensen [2] found that it took 11.5 to 15 months to get rid of tubercle bacilli in sludge drying beds but that the addition of 10 mg. of chlorine per liter of activated sludge destroys the organism. The addition of 0.5% saponated cresol solution or 0.1 to 0.2% formaldehyde solution (Formol) was also effective, but an improved low-cost method for accomplishing this purpose is urgently needed.

Perhaps the most surprising finding in Kelly's study was that the effluent from a secondary treatment plant contained Salmonella typhosa. A practical result of this finding was tracing the source back to a nursing home in which a carrier was discovered. Harvey and Phillips [3] also used exposed swabs to locate carriers of S. schottmülleri. From these studies it is seen that sewage treatment, even when complying with existing standards, does not destroy all pathogens.

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2. Peden, J. C., Jr.; Riley, J. S.; Bond, L., and Elman, R.: Blood Sugar Levels Following Intravenous Infusion of Glucose and Fructose in Adults, Metabolism **4**: 318, 1955.

3. Weichselbaum, T. E.; Margraf, H. W., and Elman, R.: Metabolism of Intravenously Infused Fructose in Man, Metabolism **2**: 434, 1953.

1. Kelly, S. M.; Clark, M. E., and Coleman, M. B.: Demonstration of Infectious Agents in Sewage, Am. J. Pub. Health **45**:1438-1446 (Nov.) 1955.

2. Jensen, K. E.: Presence and Destruction of Tubercle Bacilli in Sewage, Bull. World Health Organ. **10**:171-179, 1954.

3. Harvey, R. W. S., and Phillips, W. P.: Survival of Salmonella Paratyphi B in Sewers, Lancet **2**:137-139 (July 16) 1955.

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ORGANIZATION SECTION

FEDERAL MEDICAL LEGISLATION

Second Session, 84th Congress

Mosquito Research and Control Grants

Senator Holland (D., Fla.), in S. 2870, Congressman Fascell (D., Fla.), in H. R. 8348, and Congressman Sikes (D., Fla.), in H. R. 8400, have introduced identical bills to authorize funds "to provide for research and technical assistance relating to the control of saltmarsh and other pest mosquitoes of public health importance and mosquito vectors of human disease." The administration of funds would be vested in the surgeon general of the Public Health Service, who would establish a program to encourage states and local governments in the extermination of mosquitoes and to collect and disseminate information relating thereto. He would also conduct, in the Public Health Service, research and demonstration projects to develop methods for extermination and control of mosquitoes. Upon request from a state, he would be authorized to conduct studies and demonstrations to solve any specific mosquito problems. An annual appropriation of $2,800,000 would be authorized beginning July 1, 1956. An additional $200,000 annually would be authorized for the Department of Agriculture to investigate the effects produced on livestock by mosquitoes. The Senate bill was referred to the Committee on Labor and Public Welfare. The House measures were referred to the Committee on Interstate and Foreign Commerce.

Hospital Facilities for Retired Officers and Enlisted Men

Senator Goldwater (R., Ariz.), in S. 2898, and Congressman Rhodes (R., Ariz.), in H. R. 7956, have introduced identical measures "Directing (rather than permitting) the Administrator of Veterans' Affairs to permit retired officers and enlisted men to use available hospitals facilities . . . whenever hospital facilities over which the Veterans' Administration has direct and exclusive jurisdiction, or other Government facilities for which the Administrator of Veterans' Affairs may have contracted, are available," and the retired officer or enlisted man applies for hospital treatment for diseases or injuries. This measure was referred to the Committee on Labor and Public Welfare in the Senate and to the Committee on Veterans' Affairs in the House.

Medical Educational Facilities and Research Act of 1956

Senator Smith (R., Maine) and 29 co-sponsors, in S. 2925, and Congressman Thompson (D., N. J.), in H. R. 8556, have introduced identical measures that would authorize the expenditure of 70 million dollars a year for five years for building new medical schools or expanding or renovating existing medical schools, a total of 350 million dollars over a period of five years. The schools would be required to match the federal grants on a 50-50 basis, except in the case of new schools and in the existing schools that agree to increase their freshman enrollment 5% over the 1955-1956 figures; these would be required to match one-third to two-thirds from federal funds. Twenty per cent of the grant could be used for permanent endowment to maintain the new facility upon application to the surgeon general.

Grants (150 million dollars over five years) for medical research facilities would be authorized for accredited public and nonprofit universities and schools of medicine, dentistry, and osteopathy; hospitals; laboratories; and other public and nonprofit institutions engaged in research. This grant could be used in defraying the cost of construction. Councils would be established to advise the surgeon general in regard to the medical education facilities and medical research facilities. The Senate bill was referred to the Committee on Labor and Public Welfare and the House bill to the Committee on Interstate and Foreign Commerce.

Military Dependents Medical Care

Congressman Vinson (D., Ga.), in H. R. 7994, has introduced a measure drafted by the Department of Defense at the request of Congressman Vinson to uniformly provide medical care in government facilities and through subsidized private health insurance for the dependents of the armed forces, Public Health Service, Coast Guard, and Coast and Geodetic Survey. Medical care would continue to be given the dependents of servicemen in military medical facilities, subject to availability of space, facilities, and the capability of the military medical staff, so as not to interfere with the care of service personnel. A member of the uniformed forces could care for his dependents in a military establishment or through an insurance program, for which the serviceman would pay 30% of the premium covering a wife and children. Included would be not less than four months' hospital coverage, including the following medical care: (1) diagnosis, (2) treatment of acute medical and surgical conditions, (3) treatment of contagious diseases, (4) immunization, and (5) maternity and infant care. Excluded would be (1) home calls, except where cognizant physician considers it necessary; (2) ambulance service, except in emergencies; (3) prosthetic devices and spectacles; (4) dental treatment; (5) chronic diseases; (6) nervous and mental disorders (except for diagnostic purposes); (7) elective medical and surgical treatments; and (8) domiciliary care.

An optional health insurance plan could be offered with identical benefits for dependent parents and parents-in-law. For this, the serviceman would pay 100% of the insurance premium. The Secretary of Defense could make a charge for rates for the dependents in the military installation and require direct payments for outpatient care. In remote places and outside the continental United States, dependents could be furnished prosthetic devices and spectacles at the actual cost to the government. This measure was referred to the Committee on Armed Services.

Prepared by the Washington Office of the American Medical Association.

Federal Regulation of Health Insurance

Congressman Christopher (D., Mo.), in H. R. 8212, has introduced a measure that would prohibit insurance companies doing business of an interstate character from issuing group health, hospitalization, or accident insurance that could be canceled after three years for any reason other than nonpayment of premium. Fines for knowingly and willingly violating the law range from $1,000 to $20,000 for each and every offense. This bill was referred to the Committee on Interstate and Foreign Commerce.

Vocational Rehabilitation Study of the Homebound

Congressman Bentley (R., Mich.) proposes, in H. R. 8227, "To amend the Vocational Rehabilitation Act to provide additional Federal support to States and certain nongovernmental agencies to enable them to carry out adequate demonstration programs for the vocational rehabilitation of the homebound." The bill authorizes the expenditure of 2 million dollars annually for six years, through the Secretary of Health, Education, and Welfare for "grants to States and public and other nonprofit organizations and agencies for the purpose of '(A) establishing methods and techniques for the use of other States, organizations, and agencies in understanding the size, essential characteristics, and needs of the homebound population, (B) developing effective and economical methods for coordinating available resources to provide the services needed to achieve the highest possible level of useful activity for each physically handicapped individual who is homebound, (C) furnishing data on which reliable material estimates may be projected and the future role of the Federal Government may be determined in meeting the needs of the physically handicapped individuals who are homebound.'" This bill was referred to the Committee on Education and Labor.

Medical and Dental Officer Procurement

Congressman Vinson (D., Ga.), in H. R. 8500, has introduced a measure prepared by the Department of Defense within the Bureau of the Budget's limitations. This measure would recognize as constructive military service, for the purpose of pay and promotion, time spent in medical school and internship not to exceed five years for physicians, and four years for dentists. This would provide an immediate pay increase to medical and dental officers, depending upon the grade and amount of service, up to $76 per month. This measure was referred to the Committee on Armed Services.

WORKMEN'S COMPENSATION PUBLICATIONS

At the recent Boston meeting, the House of Delegates adopted a resolution with respect to physician selection in workmen's compensation and a guide for the evaluation and implementation of a progressive program by the medical profession. Copies of the resolution and the guide will be mailed soon to all executive secretaries of state medical societies. To help state and county medical societies who will be facing more and more opportunities for service to the occupationally disabled, the American Medical Association Council on Industrial Health has available a 96-page pamphlet entitled "Some Monetary Aspects of Workmen's Compensation." This booklet, copies of which already have been mailed to executive secretaries of state medical societies, is available at $2.50 a copy. The cost is less for bulk orders. The booklet provides the state medical societies with factual information on the trends and distribution of premiums earned and medical and indemnity losses incurred by insured employers in 39 jurisdictions for a 10-year period.

DR. PLUNKETT ON LEAVE OF ABSENCE

Dr. Richard J. Plunkett, Secretary of the American Medical Association Council on Mental Health, has been granted an extended leave of absence to serve as associate director of the newly created Joint Commission on Mental Illness and Health, Inc., with headquarters at 808 Memorial Dr., Cambridge, Mass. He will continue to serve on a part-time basis as Secretary of the Council on Mental Health. Any material or correspondence pertaining to the Council itself should be mailed to the Council at A. M. A. headquarters. The Joint Commission on Mental Illness and Health recently received the first of an eventual $1,250,000 in U. S. grants to help in a three-year national study of mental health problems. The 20 sponsoring organizations include the American Medical Association.

PHILIP MOHR HEADS DIRECTORY DEPARTMENT

Mr. Philip E. Mohr is the new director of the American Medical Association Directory-Biographical Department and is also editor of the American Medical Directory, succeeding Frank V. Cargill, who retired. Mr. Mohr joined the headquarter's staff on Feb. 1, 1954, as assistant director of the department, later becoming acting director.

ACCREDITATION OF HOSPITALS

Several months ago, Dr. E. Vincent Askey, Speaker of the American Medical Association House of Delegates, appointed a seven-man special committee to review the functions of the Joint Commission on Accreditation of Hospitals. Dr. W. C. Stover, Boonville, Ind., is chairman of the committee. Last October, the committee invited comments and suggestions from physicians relative to the commission's activities. The invitation was published in many of the state medical journals and in county medical bulletins. So far, only 164 replies from 26 states have been received. As Dr. Stover said, this is not a "big response" to such an important subject. He therefore extended the deadline for replies from Jan. 15 to March 15 and asks that any physician desiring to send his comments or suggestions do so immediately. The committee plans to meet in April and prepare its report.

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MEDICAL NEWS

CONNECTICUT

Two Lectures at Yale.—The Alpha Omega Alpha Lecture on "An Experimental Analysis of the Defense of the Host in Acute Bacterial Pneumonia" will be presented by Dr. W. Barry Wood Jr., Johns Hopkins University School of Medicine, Baltimore, at 8:15 p. m., March 13, in the Fitkin Amphitheater, Yale University School of Medicine, New Haven.——"Current Concepts of Sprue" will be delivered by Dr. Chester M. Jones, clinical professor of medicine, Harvard Medical School, Boston, in the Fitkin Amphitheater at Yale University, March 15, 8:15 p. m., under the auspices of the gastrointestinal study unit of the Yale University School of Medicine. Physicians are invited.

Fellowships in Biometry and Epidemiology.—The Yale University Graduate School, New Haven, offers predoctoral and postdoctoral fellowships, supported by a grant from the American Cancer Society, to promote training and research in biometry and statistical epidemiology. Applicants for predoctoral fellowships must be citizens of the United States who possess the degree of bachelor of arts or bachelor of science and must have a knowledge of biology, mathematics, and chemistry. They are expected to enter the graduate school as candidates for the doctor of philosophy degree and will be given training in biology and statistics. These fellowships are awarded for three years but may be terminated if the candidate fails to meet the standards of the university. Stipends will be $2,000 a year. Additional funds may be available for students with dependents. Postdoctoral fellowships are intended for young men and women embarking on an investigative career and also for more mature investigators desiring to extend their fields of competence. Candidates must be citizens of the United States who possess the degree of doctor of medicine, doctor of philosophy, or doctor of science. Fellows will be given training in biometry, biostatistics, and such other subjects as the university may deem necessary. Fellowships, awarded for periods of one year, may be renewed for two additional years. The stipends will range from $3,500 to $4,500, depending on individual circumstances. For information write to E. Cuyler Hammond, Sc.D., Director, Graduate Studies in Biometry, 30 Hillhouse Ave., Yale University, New Haven. Applications for both types of fellowships should be submitted as early as possible.

FLORIDA

Hospital News.—Dr. Leo Loewe, clinical professor of medicine, State University of New York College of Medicine at New York City, Brooklyn, and president, American College of Angiology, was the annual guest lecturer of the Educational Fund of Mount Sinai Hospital of Greater Miami, funds for which were donated by the Wohl Foundation. Dr. Loewe gave an informal talk entitled "What's New in Antibiotics."

Postconvention General Practice Congress.—After the close of the eighth annual scientific assembly of the American Academy of General Practice in Washington, D. C. (see General News), the 1956 Invitational Scientific Congress will be held March 24 at the Fontainbleau Hotel, Miami Beach, under the sponsorship of the Dade County and Florida chapters of the academy. There will be a $10 registration fee for visiting doctors. Attendance by members will qualify them for category 1 postgraduate study credit. The scientific program, which will be held during the afternoon only, will be presented by Dr. John H. Mickley, Hollywood, who will discuss "The Woes of a Pathologist"; Dr. Kermit H. Gates, director of the Jackson Memorial Hospital, Miami, who will present a paper on "A Dissection of the Head by the Public Health Officer for the General Practitioner"; Dr. Robert B. Lawson, professor of pediatrics, University of Miami, whose topic will be "To Treat or Not to Treat"; and Dr. Bernard Goodman, attending psychiatrist at Jackson Memorial Hospital, Miami, who has been invited to discuss "The Office Couch." At the banquet, 7 p. m., the guest speaker will be Dr. Leo M. Wachtel, Jacksonville, president-elect of the Florida chapter, with the subject of "A Backward Glance at General Practice."

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

GEORGIA

Convention on Clinical Endocrinology.—Physicians in the southeastern states have been invited to attend a convention on clinical endocrinology at the Georgia Hotel, Atlanta, March 19-20. The speaker, Dr. Philip K. Bondy, associate professor of internal medicine, Yale University School of Medicine, New Haven, Conn., was formerly affiliated with the Emory University School of Medicine, Emory University, and with the Harvard Medical School, Boston. The meeting is sponsored by the Lanpar Company, pharmaceutical manufacturers of Dallas, Texas.

Symposium on Congenital Heart Disease.—A symposium on the diagnosis and treatment of congenital heart disease will be held March 22-24 at the Academy of Medicine, 875 W. Peachtree St., N. E., Atlanta, under the sponsorship of the Medical College of Georgia, Augusta, Emory University School of Medicine, Emory University, the state health department, and Georgia Heart Association. The symposium is designed for internists, radiologists, and thoracic surgeons. Participants will include Dr. C. Walton Lillehei of the University of Minnesota Medical School, Minneapolis; Dr. Edward B. D. Neuhauser, Children's Medical Center, Boston; and Dr. S. Gilbert Blount Jr., University of Colorado School of Medicine, Denver. For information write to Dr. J. Gordon Barrow at 1123 Gordon St., S. W., Atlanta.

ILLINOIS

Society News.—The following surgeons were recently elected to the executive council of the International College of Surgeons (1516 Lake Shore Dr.): Drs. George F. Lull, Edward L. Compere, Jacob P. Greenhill, Morris L. Parker, Philip B. Thorek, Jerome J. Moses, Fritz R. Rothbart, and Ulysses G. Dailey, all of Chicago, and Dr. Louis F. Plzak of Berwyn.

Radioactive Isotopes in Clinical Medicine.—At the meeting of the Adams County Medical Society in the Hotel Lincoln-Douglas, Quincy, March 12, 7:45 p. m., Donalee L. Tabern, Ph.D., Chicago, head, department of radioactive pharmaceuticals, Abbott Laboratories, will present a paper on the use of radioactive isotopes in the diagnosis and treatment of disease. Visiting physicians are invited.

Seminar in Psychiatry.—In its series of seminars on "Modern Concepts in Psychiatry," the Veterans Administration Hospital, Downey, will present "Medical Orientation in Society" March 14. A case presentation will be made at 1 p. m. The speaker will be Dr. C. H. Hardin Branch, professor of psychiatry and head of the department of psychiatry and neurology, Salt Lake County General Hospital, Salt Lake City.

Grants in Rheumatology.—The medical and scientific committee of the Illinois chapter of the Arthritis and Rheumatism Foundation is accepting applications for research grants in rheumatology and the basic sciences. Application blanks may be secured from the chapter office at 1009 N. State St. (telephone, WHitehall 4-0244). Completed applications (in duplicate) must be in the chapter office no later than March 15.

Golden Anniversary of Tuberculosis Institute.—The Tuberculosis Institute of Chicago and Cook County will celebrate its 50th anniversary at the seventh annual spring conference March 14-16 in the Hotel Sherman, Chicago. After the address of

welcome by Mr. Herbert C. De Young, president, Dr. Warren W. Furey, vice-president, will preside over the morning program:

The World We Live In, Morris Fishbein, Chicago.
Highlights of Fifty Years of Organized Effort, Walter C. Bornemeier, Chicago.
The Hardest Fifty Years—Ahead, James E. Perkins, New York City.

Tuberculosis Control Problems in Metropolitan Areas will be presented at the afternoon session, over which Dr. Ernest E. Irons, Chicago, will preside and which will include consideration of "Many People, Many Diseases, Many Problems" by Dr. Herman N. Bundesen, president, Chicago Board of Health. A case-finding session is scheduled for Thursday morning (Dr. Edward A. Piszcek, Forest Park, presiding). The following presentations will be made:

A New Look at an Old Weapon—the Tuberculin Test, Floyd M. Feldman.
Our Big Gun—the Mass Survey, Meyer R. Lichtenstein, Chicago.
General Hospitals and Clinics—a Problem of Logistics, David B. Radner, Winfield.
In the Front Line—the Private Physician, Eugene T. McEnery, Chicago.
Hits or Misses? Herbert S. Ratner, Oak Park, Ill.

Dr. Otto L. Bettag, director, Illinois Department of Public Welfare, will preside at the Thursday morning session, which will have as its theme "Rehabilitation—Now Is Tomorrow." Thursday afternoon will be devoted to a joint meeting of the institute and the Chicago Tuberculosis Society, with Dr. Robert O. Levitt, president of the society, presiding over the following program:

Treatment of Primary Tuberculosis, Edna M. Jones, Northville, Mich.
Pulmonary Surgery—a Critical Review, William M. Tuttle, Detroit.
Fungus Disease, Michael L. Furcolow, Kansas City, Kan.

The conference will end with a luncheon Friday, preceded by a panel discussion (How Can We Work Together for Effective Education?) in which Dr. George C. Turner, Oak Forest, will participate.

Chicago

Meeting on Cardiology.—The Chicago Heart Association will present a symposium on misdiagnoses, March 13, 8 p. m., at the Drake Hotel (SU 7-2200). All physicians are welcome. After presentation of cases by Drs. Aaron B. Shaffer, Medical Research Institute, Michael Reese Hospital; David W. Hines, Veterans Administration Research Hospital; and William L. Deardorff and Steven J. Spinnuzza, Cook County and Ravenswood hospitals, Dr. Aldo A. Luisada, associate professor of medicine, division of cardiology, Chicago Medical School, will give the summary.

Society News.—At its meeting March 14, 8 p. m., in the Chicago Medical School, 710 S. Wolcott St., the Chicago Society of Physical Medicine and Rehabilitation will hear Dr. Meyer A. Perlstein discuss "Clinical Correlations in Cerebral Palsy." The scientific session will be preceded by a dinner meeting, 6:30 p. m., at University Inn, 1824 W. Harrison St. ($3.50 per person).——At the meeting March 12, 7:30 p. m., at the Drake Hotel, the Chicago Pathological Society will present "The Basic Pathology of Leprosy" by Dr. Olaf K. Skinsnes; "Acceleration of the Development of 'AKR Lymphoma' by Means of Cell-Free Filtrates" by Drs. Steven O. Schwartz, Harold M. Schoolman, and Paul B. Szanto; and a cinema demonstration of necropsy and embalming techniques by the Chicago Funeral Directors' Association. The society also announces that the fourth Ludvig Hektoen Commemorative Services will be held at the Hyde Park Baptist Church, March 18, 11 a. m.

MICHIGAN

Society News.—On March 13 at 8:15 p. m., the Henry Ford Hospital Medical Society will present in the hospital auditorium "New Work on Pain" by Dr. Henry K. Beecher, Dorr Professor of Research in Anesthesia, Harvard Medical School, Boston.

Plays Dealing with Family Problems.—Wayne University Theatre and the Michigan Society for Mental Health announce that, through a new program service, the Wayne University Theatre Family Plays, productions of five plays dealing with family problems, have been made available free of charge to organizations in the Detroit metropolitan area. The plays, written for the American Theatre Wing, which has been presenting them for several years in the New York City area, are designed to be followed by a discussion period, stimulated by the problems dramatized. The plays are: "And You Never Know" (a crisis between a jealous sister and her family); "The Room Upstairs" (tensions between a grandmother and her resentful children); "Random Target" (portrayal of an overly aggressive child, the victim of harsh punishment); "Tomorrow Is a Day" (destruction of a teen-age girl's confidence); and "Scattered Showers" (three preschool children faced with danger). Requests for information should be addressed to the Michigan Society for Mental Health, 153 E. Elizabeth, Detroit.

MONTANA

State Medical Interim Session.—The Montana Medical Association will hold its ninth annual interim session in Helena, March 16-17 under the presidency of Dr. George W. Setzer, Malta. The scientific session will be held Friday at the Veterans Administration Center, Fort Harrison, where the program will feature a series of clinical conferences in cardiology, ophthalmology and otolaryngology, orthopedics, pediatrics, obstetrics and gynecology, vasomotor disturbances, radiology, sigmoidoscopy, urology, surgery, and dermatology. Dr. Gertrude L. Pease, Rochester, Minn., has been invited to talk on hematology and to participate in a clinical pathological conference. She will be sponsored by the Montana division of the American Cancer Society. At the banquet Friday, 7:30 p. m., Dr. Setzer will serve as toastmaster. Dr. M. Shelby Jared, Seattle, medical director of the King County (Wash.) Medical Service Bureau and immediate past-president of the Washington State Medical Association, will deliver an address, "The Physician, the Government, and Prepayment."

NEW JERSEY

Doctors' Chorus.—On March 14 at the New York Athletic Club, the Doctors' Chorus will join with the Associated Glee Clubs of Greater New York in a jamboree of choral music. The season's work is expected to end May 9, the date of the seventh annual Benefit Concert for the Chronically Ill.

Society News.—Newly elected officers of the New Jersey Diabetes Association include: Dr. Otto Brandman, president; Dr. Louis Grunt, vice-president; Dr. William Levison, secretary; and Dr. John J. Torppey, treasurer, all of Newark.——Newly elected officers of the Society of Surgeons of New Jersey include: Dr. William H. McCallion, Elizabeth, president; Dr. David B. Allman, Atlantic City, first vice-president; Dr. Rocco M. Nittoli, Elizabeth, second vice-president; Dr. John L. Varriano, Jersey City, secretary; and Dr. Leo H. Salvati, Westfield, treasurer.

NEW YORK

Course in Hospital Administration.—Next fall Cornell University, Ithaca, will inaugurate a program in hospital administration. The Sloan Institute of Hospital Administration will have among its primary aims the training of a select number of students in a hospital administration program leading to a master's degree and the development of a long-range research program in hospital studies. The program in hospital administration will be a cooperative venture of the faculty of the Graduate School of Business and Public Administration. Hospital administration students will participate with students majoring in business as well as those majoring in public administration in the first-year curriculum in administrative science. Advanced second-year training will be given in the several subjects related to health and hospital administration, reflecting the major research activities of the faculty in hospital studies. The two years of course work will be followed by a year of supervised hospital residency. Completion of this program qualifies the student for the degree of master of public administration or master of business administration in hospital management. Six fellowships of $2,500 are available. Smaller awards will be made when circumstances do not require grants of $2,500. For details write to: Administrative Secretary, Graduate School of Business and Public Administration, Cornell University, Ithaca, N. Y. Applications for awards must be submitted by April 15.

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New York City

Charles H. May Memorial Lecture.—Dr. Edwin B. Dunphy, Boston, will deliver the annual Charles H. May Memorial Lecture (sponsored by the section of ophthalmology of the New York Academy of Medicine) at the academy March 19 on "Radioactive Isotopes in Ophthalmology."

Harvey Lecture.—Keith R. Porter, Ph.D., associate member, Rockefeller Institute for Medical Research, will deliver the seventh Harvey Lecture of the 1955-1956 series at the New York Academy of Medicine March 15, 8:30 p. m., on "The Submicroscopic Morphology of Protoplasm."

Course on Gynecology and Endocrinology.—The interrelationship of the glands of internal secretion and various gynecologic problems will be the principal topic of a course to be given full-time during the week of April 9 by the Post-Graduate Medical School, a unit of the New York University-Bellevue Medical Center, under the joint direction of Drs. Herbert S. Kupperman and Theodore Neustaedter. Topics for discussion include adrenal cortical factors in gynecology; complications and management of menopause, dysmenorrhea, menstrual irregularities, and hypermenorrheas; and related problems.

OHIO

Postgraduate Course at Cleveland.—The Frank E. Bunts Educational Institute affiliated with the Cleveland Clinic Foundation announces a postgraduate course, "Medical Progress and Its Relationship to Dentistry," March 14-15, sponsored by the Cleveland Dental Society. The program will be presented in the North Clinic Building (Euclid Avenue and East 93rd Street) by staff members of the Cleveland Clinic Foundation, members of the Cleveland Dental Society, and guest speakers. It will end with a panel discussion, "Advances in Medicine and Dentistry," moderated by Thomas J. Hill, D.D.S., professor emeritus, oral pathology, Western Reserve University School of Dentistry, Cleveland, with Dr. Wallace D. Armstrong, professor and head of the department of physiological chemistry, University of Minnesota Medical School, Minneapolis; Dr. Arthur C. Ernstene; A. H. Kniesner, D.D.S., assistant professor of pathology and peridontia, Western Reserve School of Dentistry, Cleveland; and Dr. Ernest P. McCullagh, Cleveland, as collaborators. The registration fee is $15, except for interns and residents and members of the armed forces in uniform, who will be admitted free.

PENNSYLVANIA

Personal.—Dr. Joseph C. Atkins, who at the age of 84 is still in practice in Red Lion, recently presented a testimonial plaque from the Medical Society of the State of Pennsylvania to one of his patients, Mrs. Annie M. Shelley, Stewartstown, on her 100th birthday. Dr. Atkins, who has practiced in Red Lion since 1898, has two sons who are physicians.

"Help the Busy Doctor."—The Woman's Auxiliary of the Medical Society of the State of Pennsylvania will hold its 10th annual midyear conference at the Penn-Harris Hotel, Harrisburg, March 12-14. The theme of the meeting will be "Help the Busy Doctor." Physicians who will participate in the conference include Dr. Edward J. Carroll, associate professor of psychiatry, University of Pittsburgh, who will be the guest speaker at the Tuesday luncheon; Dr. E. Roger Samuel, Mount Carmel, general practitioner of the year, guest at the dinner, Tuesday, 6 p. m.; Dr. Allen W. Cowley, Harrisburg, who will moderate a panel Wednesday, 9:20 a. m. on "How to Help the Busy Doctor"; and Dr. C. L. Palmer, Pittsburgh, who will speak on critical legislation Wednesday, 10:40 a. m.

Philadelphia

Phi Delta Epsilon Lecture.—The Beta Zeta chapter of Phi Delta Epsilon Fraternity at Hahnemann Medical College and Hospital of Philadelphia will sponsor its ninth annual lecture March 14. Dr. Jerome A. Urban of the Presbyterian Hospital in New York City will discuss "The Importance of the Internal Mammary Nodes in Carcinoma of the Breast."

TEXAS

Clinical Conference at Dallas.—The Dallas Southern Clinical Society will hold its spring clinical conference March 12-14 in 433 Medical Arts Bldg., Dallas. Honor guests will include Drs. Franz Altmann, Victor F. Marshall, and Philip D. Wilson Sr., New York; Drs. Walter Bauer, Richard B. Cattell, Trygve Gundersen, Samuel A. Levine, Laurence L. Robbins, Boston; Drs. Granville A. Bennett and William J. Dieckmann, Chicago; Dr. Jack S. Guyton, Detroit; Dr. Thaddeus L. Montgomery, Philadelphia; Drs. Paul J. Moses and Robert A. Scarborough, San Francisco; Dr. Ralph M. Patterson, Columbus, Ohio; Dr. H. Marvin Pollard, Ann Arbor, Mich.; Dr. James D. Rives, New Orleans; and Dr. Lawson Wilkins, Baltimore.

Meeting of Neurological Society.—The fourth annual scientific session of the Houston Neurological Society will be held March 16-17 at the Jesse H. Jones Library Building, Texas Medical Center, Houston. The first day will be devoted to the following symposium, Brain Mechanisms and Drug Action:

- Neurophysiology of the Reticular System, Robert S. Livingston, department of anatomy, University of California Medical Center, Los Angeles.
- Effect of Drugs on the Reticular System, Harold E. Himwich, director, research division, Galesburg (Ill.) State Research Hospital.
- Effect of Drugs on Neurons and Synapses: (1) Amedeo S. Marrazzi, chief, clinical research division, Army Chemical Center, Md.; (2) Eva King Killam, Ph.D., department of anatomy, University of California Medical Center, Los Angeles.
- Effect of Drugs on Behavior, Joseph V. Brady, chief, department of experimental psychology, Walter Reed Army Institute of Research, Washington, D. C.
- Summary of Day's Activities, Ralph W. Gerard, mental health research division, University of Michigan Hospital, Ann Arbor, Mich.

The program on the second day will consist of clinical and basic science papers in neurology and neurosurgery.

GENERAL

Annual Cancer Campaign.—The American Cancer Society has chosen as the theme of its 1956 fund-raising campaign "Strike back at cancer with a checkup and a check." The society will open its 26-million-dollar crusade in April.

Oto-Ophthalmologists Meet in Omaha.—The Omaha and Council Bluffs (Iowa) Ophthalmological and Otolaryngological Society and the Nebraska Academy of Ophthalmology and Otolaryngology will hold a joint all-day session in Omaha on March 15. The principal speaker for ophthalmology will be Dr. Harold G. Scheie, Philadelphia, and the principal speaker for otolaryngology Dr. George E. Shambaugh Jr., Chicago. Members of the neighboring eye, ear, nose, and throat societies have been invited. The Kansas City Society of Ophthalmology and Oto-Laryngology plans to attend as a group.

Psychology in Medical Education.—A conference on this subject will be held in New York City, March 12-14. The meetings will be attended by psychologists from medical schools and representatives of the American Psychological Association, the Association of American Medical Colleges, and the Veterans Administration. The program will include work groups on teaching, research, clinical service, and selection and administration. Information may be obtained from Irwin J. Knopf, Ph.D., Chairman, Committee on Publicity and Publications, Department of Psychiatry, State University of Iowa College of Medicine, Iowa City.

Surgeons Meet in Little Rock.—The American College of Surgeons will hold a sectional meeting March 12-13 at the Hotel Marion, Little Rock, Ark., under the chairmanship of Dr. Joseph F. Shuffield, Little Rock. The sessions will open with a symposium on the management of mass casualties. Other symposiums will include trauma, surgery of the aged, cancer, and the acute abdomen. Panel discussions have been scheduled on fluid balance and biliary tract surgery. Guest speakers will include Dr. James A. Kirtley Jr., Nashville, Tenn.; Dr. William M. Tuttle, Detroit; Dr. Warren H. Cole, Chicago; Drs. James B. Hartgering and Joseph R. Shaeffer, Washington, D. C.; Dr. Robert H. Kennedy, New York; Dr. William J. Engel, Cleveland; Dr. James M. Mason III, Birmingham, Ala.; and Dr. B. Marden Black, Rochester, Minn.

UNIVERSITY OF MICHIGAN LIBRARIES

Meeting of Orthopsychiatric Association.—The 33rd annual meeting of the American Orthopsychiatric Association will convene at the hotels Commodore and Roosevelt, New York City, March 15-17. The principal topics of discussion will be juvenile delinquency, mental health in schools, psychiatric treatment of children, psychiatric clinic practices and procedures, and adult psychotherapy. In all, 65 scientific papers and 20 workshop sessions will be presented. The general session will open Thursday at 10 a. m. with "Challenge to Orthopsychiatry: Professional Perspectives" by Dr. Exie E. Welsch, New York City, president. Discussions on ambulatory (borderline) schizophrenia will open the Friday morning and afternoon sessions. A symposium on orthopsychiatry and problems of learning will be held Saturday morning. Most sessions will be open to nonmembers. Registration fee for nonmembers is $2 a day or $5 for three days.

Rehabilitation Workshop.—Applications are being accepted for the third annual practical workshop on "Team Concepts and Techniques in Rehabilitation," May 28-June 22, at the Institute for the Crippled and Disabled in New York City, conducted jointly with Columbia University. The course will include seminars in rehabilitation philosophy and principles, continuous case seminars conducted by the enrollees, and participation in the presentation of certain cases to the student seminar and to the institute's staff case conference. Lectures and discussions by guest specialists and visits to other rehabilitation facilities in the New York area will be included. Persons in the following categories will be considered for enrollment: physiatrists, psychiatrists and other medical specialists, psychologists, social workers, vocational counselors, placement workers, physical therapists, special educators, occupational therapists, workshop supervisors, administrators, speech therapists, and group workers. Enrollment will be limited to 25. The fee for the course, $100, does not cover transportation and living costs. The institute is endeavoring to arrange for a limited number of stipends payable at the conclusion of the course to help defray travel and residence expenses for those whose residency changes in connection with the course would work a financial hardship. Information may be had from Dr. Abraham Jacobs, Department of Psychological Foundations and Services, Teachers College, Columbia University, New York 27.

General Practice Meeting in Washington.—The eighth annual scientific assembly of the American Academy of General Practice will convene March 19-22 at the District of Columbia National Guard Armory, Washington, D. C. The scientific session will open at 1:30 p. m. Monday with "Disturbances and Distortions of Demeanor" by Dr. Mabel L. Ross, consultant, U. S. Public Health Service, New York; Dr. Robert H. Felix, National Institute of Mental Health, Bethesda, Md.; Dr. George N. Raines, Georgetown University School of Medicine, Washington, D. C.; and Dr. Manfred S. Guttmacher, chief medical officer (psychiatric adviser), Supreme Bench of Baltimore. At 4 p. m. the Rev. Das Kelley Barnett, Austin, Texas, will discuss "Medicine and Religion." The Monday session will end with "The Changing Pattern of Disease" by Dr. Leonard A. Scheele, surgeon general, Public Health Service, Washington, D. C. A symposium on modern day obstetrics is scheduled for Wednesday, 1:30 p. m. Dr. Robert H. Barter, Washington, D. C., will discuss preparation for the pregnancy; Dr. Paul A. Bowers, Philadelphia, will speak on protecting the pregnancy; and Dr. D. Frank Kaltreider, Baltimore, will have as his subject preserving the perineum. The president's reception and dance will be held Wednesday evening at the Hotel Statler. The incoming president, Dr. John S. DeTar, Milan, Mich., will be installed at 8 p. m. The scientific sessions will close Thursday with presentation at 11:30 a. m. of "A Look at Tomorrow's Medicine" by Dr. Francis C. Wood, Philadelphia. Tours to the National Institutes of Health, Bethesda, Md., have been arranged for Thursday afternoon.

Postgraduate Courses Not Previously Published.—March 19, a postgraduate conference in **ophthalmology** will be offered by Stanford University School of Medicine, Stanford University-San Francisco. This will be a five-day concentrated course at the medical school for specialists in ophthalmology at a fee of $100. March 26, a postgraduate conference in **otorhinolaryngology** will be offered by the Stanford University School of Medicine. This will be a concentrated five-day course for specialists in the field at a fee of $100. The enrollment will be limited to 30 physicians. March 20, the University of Wisconsin School of Medicine, Madison, will offer a postgraduate course in **internal medicine.** This will be a concentrated three-day course for physicians in both general and in specialty practice at a fee of $20. Enrollment will be limited to 45 physicians. April 16, a postgraduate course in **cardiology** will be given at the St. Francis Hospital and Sanatorium, Roslyn, N. Y. This will be a concentrated two-week course for physicians both in general and in specialty practice, at a fee of $35. Enrollment will be limited to 60 physicians. May 9, the fourth biennial **cardiovascular seminar** will take place in the Eden Roc Hotel, Miami Beach, Fla. This will be a concentrated four-day lecture course for specialists in internal medicine at a fee of $20. Inquiries should be addressed to the Heart Association of Greater Miami, 313 Calumet Building, Miami, Fla. May 28, an intensive review of **surgical anatomy** will be offered by Cornell University Medical College, New York. This concentrated four-week course for specialists will include dissection, at a fee of $200. Enrollment will be limited to 25.

Surgical Congress in Richmond.—The Southeastern Surgical Congress will hold its 24th annual meeting March 12-15 at the John Marshall Hotel, Richmond, Va. Panel discussions have been scheduled on bones, stomach, colon, and blood vessels. Dr. Elmer Hess, Erie, Pa., President of the American Medical Association, will deliver an address. Presentations by other guest speakers will include:

Arthur H. Blakemore, New York City, Progress in the Development of Arterial Prostheses.
Alexander Brunschwig, New York City, Some Favorable Results in Supraradical Surgery for Advanced Upper Abdominal Cancer.
R. Lee Clark Jr., Houston, Texas, Principles of Cancer Surgery.
Bradley L. Coley, New York City, Resection in the Treatment of Tumors of Bone.
Frederick A. Coller, Ann Arbor, Mich., Surgery in the Aged.
Denton A. Cooley, Houston, Texas, Excisional Treatment of Aortic Aneurysms.
Irving S. Cooper, New York City, Neurosurgical Alleviation of Parkinsonism.
William L. Estes Jr., Bethlehem, Pa., Five-Year End-Results Following Repair of Inguinal Hernia.
George A. Higgins, Kansas City, Mo., Surgery of the Adrenal Gland.
J. William Hinton, New York City, Clinical and Experimental Studies to Determine the Role of the Pancreas in Serum Amylase Formation.
Henry A. Kingsbury, New York City, Cancer of the Thyroid Gland.
Stanford W. Mulholland, Philadelphia, Diverticulum of the Urethra in the Female.
George T. Pack, New York City, Diagnosis and Treatment of Sarcomas of the Soft Tissues.
Robert A. Robinson and George Smith, Baltimore, Treatment of Certain Cervical Spine Disorders by Anterior Disc Removal and Interbody Arthrodesis.
James E. Thompson, New York City, Surgical Significance of Polyps of the Colon.
William Crawford White, New York City, Indications for Radical Mastectomy Versus Less Extensive Surgery.
Robert M. Zollinger, Columbus, Ohio, Surgery of the Spleen.

FOREIGN

Course on Social Pediatrics.—The International Children's Centre (Chateau de Longchamp, Bois de Boulogne, Paris XVIe) will present the ninth course of social pediatrics April 9-July 1. The course, which will be attended by 35 students from 30 countries, is especially intended for physicians in charge of carrying out joint programs of the United Nations Children's fund, the World Health Organization, and the governments of various countries.

International Congress of Medical Radiophotography.—The second International Congress of Medical Radiophotography will be held in Paris, France, April 4-7. The provisional program provides for radiophotography in pulmonary tuberculosis; radiophotography in nontuberculous diseases of the thorax and in its new applications outside thoracic diseases; apparatus and techniques in radiophotography; and the reading and interpretation of radiophotographic films. Information may be obtained from the Secretariat, 66 Boulevard Saint-Michel, Paris 6ème.

Residency Posts for Doctors from India.—The Indian Medical Association requests offers from recognized hospitals for residency posts in all specialties for doctors from India (men and women), specially selected for graduate training in hospitals in the United States. These physicians will have a good command of spoken and written English. The hospitals must be approved by the U. S. State Department for the exchange visitor program. Interested hospitals are requested to communicate by air mail with the Honorary Secretary, Indian Medical Association, "Hanging Bridge," Daryaganj, Delhi 7, India, giving offers of posts, terms of appointment, maintenance, stipend, and the allotted number for the exchange visitor program.

Congresses on Orthopedic and Traumatic Surgery.—In its seminar congresses in orthopedic and traumatic surgery, the American Medical Society of Vienna will present the following programs by the Medical Faculty of the University of Vienna:

May 17-18, Treatment of Congenital Orthopedic Deformation.
June 21-22, Fractures of the Extremities.
July 19-20, Rehabilitation.
Aug. 23-24, Surgical Treatment of Joints.
Sept. 20-21, Intramedullary Nailing.
Oct. 18-19, Cranial and Spinal Injuries.
Nov. 22-23, Surgical Treatment of the Hand.

Details may be obtained from the American Medical Society of Vienna, Vienna I, Universitaetsstrasse 11, Cable: "AMMEDIC," Vienna.

CORRECTION

Guest Editorial.—In the editorial "Histaminic Cephalalgia" in THE JOURNAL, Feb. 11, page 468, the first footnote erroneously stated that Dr. Bayard T. Horton was head secretary in the division of medicine at the Mayo Clinic. The footnote should have stated that Dr. Horton is head of a section of medicine at the Mayo Clinic and an associate professor of medicine at the Mayo Foundation, Graduate School, University of Minnesota.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1956 Annual Meeting, Chicago, June 11-15.
1956 Clinical Meeting, Seattle, Nov. 27-30.
1957 Annual Meeting, New York, June 3-7.
1957 Clinical Meeting, Philadelphia, Dec. 3-6.
1958 Annual Meeting, San Francisco, June 23-27.
1958 Clinical Meeting, Minneapolis, Dec. 2-5.

AERO MEDICAL ASSOCIATION, Drake Hotel, Chicago, Apr. 16-18. Dr. Thomas H. Sutherland, P. O. Box 26, Marion, Ohio, Secretary.

ALABAMA, MEDICAL ASSOCIATION OF THE STATE OF, Birmingham, Apr. 19-21. Dr. Douglas L. Cannon, 537 Dexter Ave., Montgomery, Secretary.

AMERICAN ACADEMY OF GENERAL PRACTICE, Hotel Statler, Washington, D. C., Mar. 19-22. Mr. Mac F. Cahal, Broadway at 34th Street, Kansas City 11, Mo., Executive Secretary.

AMERICAN ACADEMY OF NEUROLOGY, Hotel Jefferson, St. Louis, Apr. 23-28. Dr. Thomas W. Farmer, Dept. of Medicine, University of North Carolina, Chapel Hill, N. C., Secretary.

AMERICAN ACADEMY OF PEDIATRICS, Rice Hotel and Sam Houston Coliseum, Houston, Texas, Apr. 16-19. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Illinois, Executive Secretary.

AMERICAN ASSOCIATION OF ANATOMISTS, Milwaukee, Apr. 4-6. Dr. Normand L. Hoerr, 2109 Adelbert Rd., Cleveland 6, Secretary.

AMERICAN ASSOCIATION FOR HEALTH, PHYSICAL EDUCATION, RECREATION, Conrad Hilton Hotel, Chicago, Mar. 24-30. Mr. Carl A. Troester Jr., 1201 Sixteenth St., N.W., Washington 6, D. C., Executive Secretary.

AMERICAN ASSOCIATION OF THE HISTORY OF MEDICINE, Washington Duke Hotel, Durham, N. C., Apr. 19-26. Dr. Ilza Veith, 950 East 59th St., Chicago 37, Executive Secretary.

AMERICAN ASSOCIATION OF IMMUNOLOGISTS, Chalfonte-Haddon Hall, Atlantic City, N. J., Apr. 16-20. Dr. F. S. Cheever, Univ. of Pittsburgh, School of Public Health, Pittsburgh 13, Secretary.

AMERICAN ASSOCIATION OF PATHOLOGISTS AND BACTERIOLOGISTS, Netherland Plaza Hotel, Cincinnati, Apr. 26-28. Dr. Edward A. Gall, Dept. of Pathology, Cincinnati General Hospital, Cincinnati 29, Secretary.

AMERICAN ASSOCIATION OF RAILWAY SURGEONS, Drake Hotel, Chicago, Apr. 10-12. Dr. Chester C. Guy, 5800 Stony Island Ave., Chicago 37, Secretary.

AMERICAN COLLEGE OF ALLERGISTS, Hotel New Yorker, New York, Apr. 15-20. Dr. Fred W. Wittich, 401 Marquette Bank Bldg., Minneapolis 2, Secretary.

AMERICAN COLLEGE OF PHYSICIANS, Los Angeles, Apr. 16-20. Mr. E. R. Loveland, 4200 Pine St., Philadelphia 4, Executive Secretary.

AMERICAN FEDERATION FOR CLINICAL RESEARCH, Chalfonte-Haddon Hall, Atlantic City, N. J., April 29. Dr. William W. Stead, VA Hospital, Minneapolis 17, Secretary.

AMERICAN GASTROENTEROLOGICAL ASSOCIATION, Claridge Hotel, Atlantic City, N. J., Apr. 27-28. Dr. H. Marvin Pollard, University Hospital, Ann Arbor, Mich., Secretary.

AMERICAN GERIATRICS SOCIETY, Palmer House, Chicago, May 3-4. Dr. Malford W. Thewlis, 25 Mechanic St., Wakefield, R. I., Secretary.

AMERICAN GOITER ASSOCIATION, Drake Hotel, Chicago, May 3-5. Dr. John C. McClintock, 149½ Washington Ave., Albany 10, N. Y., Secretary.

AMERICAN ORTHOPSYCHIATRIC ASSOCIATION, Hotel Commodore, New York, Mar. 15-17. Dr. Marion F. Langer, 1790 Broadway, New York 19, Executive Secretary.

AMERICAN PHYSIOLOGICAL SOCIETY, Atlantic City, N. J., Apr. 16-20. Dr. Allan C. Burton, University of Western Ontario, London, Ontario, Canada, Secretary.

AMERICAN PSYCHIATRIC ASSOCIATION, Chicago, April 30-May 4. Dr. William Malamud, 80 East Concord St., Boston 18, Secretary.

AMERICAN PSYCHOSOMATIC SOCIETY, Sheraton Plaza, Boston, Mar. 24-25. Dr. Theodore Lidz, 333 Cedar St., New Haven 11, Conn., Secretary.

AMERICAN RADIUM SOCIETY, Shamrock Hotel, Houston, Texas, Apr. 9-11. Dr. Robert E. Fricke, 102 Second Ave. S.W., Rochester, Minn., Secretary.

AMERICAN SOCIETY FOR ARTIFICIAL INTERNAL ORGANS, Atlantic City, N. J., Apr. 15-16. Dr. Peter F. Salisbury, Institute for Medical Research, 4751 Fountain Ave., Los Angeles 29, Secretary.

AMERICAN SOCIETY OF BIOLOGICAL CHEMISTS, Atlantic City, N. J., Apr. 15-19. Dr. Philip Handler, Duke University, Durham, N. C., Secretary.

AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, Chalfonte-Haddon Hall, Atlantic City, N. J., April 30. Dr. J. D. Myers, University of Pittsburgh School of Medicine, Pittsburgh 13, Secretary.

AMERICAN SOCIETY FOR EXPERIMENTAL PATHOLOGY, Atlantic City, N. J., Apr. 15-21. Dr. Cyrus C. Erickson, 874 Union Ave., Memphis 3, Tenn., Secretary.

AMERICAN SOCIETY OF MAXILLOFACIAL SURGEONS, Jung Hotel, New Orleans, Mar. 18-21. Dr. John A. Drummond, 1414 Drummond St., Montreal, Canada, Secretary.

AMERICAN SOCIETY FOR PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, Atlantic City, N. J., Apr. 15-20. Dr. Carl C. Pfeiffer, Emory University School of Medicine, Emory University, Ga., Secretary.

AMERICAN SURGICAL ASSOCIATION, The Greenbrier, White Sulphur Springs, W. Va., Apr. 11-13. Dr. R. Kennedy Gilchrist, 59 East Madison St., Chicago 3, Secretary.

ARIZONA MEDICAL ASSOCIATION, San Marcos Hotel, Chandler, Apr. 25-28. Dr. D. W. Melick, 411 Security Bldg., Phoenix, Secretary.

ARKANSAS MEDICAL SOCIETY, Hotel Marion and Robinson Auditorium, Little Rock, Apr. 23-25. Mr. Paul C. Schaefer, 213 Kelley Bldg., Ft. Smith, Executive Secretary.

ASSOCIATION OF AMERICAN PHYSICIANS, Chalfonte-Haddon Hall, Atlantic City, N. J., May 1-2. Dr. Paul B. Beeson, Yale University School of Medicine, New Haven 11, Conn., Secretary.

ASSOCIATION OF AMERICAN PHYSICIANS AND SURGEONS, Columbus, Ohio, Apr. 5-7. Dr. William L. Baughn, 1635 West 25th St., Anderson, Ind., Secretary.

CALIFORNIA MEDICAL ASSOCIATION, Ambassador Hotel, Los Angeles, April 29-May 2. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

CONNECTICUT STATE MEDICAL SOCIETY, Hamden, Apr. 24-26. Dr. Creighton Barker, 160 St. Ronan St., New Haven, Executive Secretary.

DALLAS SOUTHERN CLINICAL SOCIETY, Dallas, Tex., Mar. 12-14. Miss Helga Boyd, 433 Medical Arts Bldg., Dallas 1, Tex., Executive Secretary.

EASTERN CONFERENCE OF RADIOLOGISTS, Lord Baltimore Hotel, Baltimore, Mar. 15-17. Dr. Richard B. Hanchett, 705 Medical Arts Bldg., Baltimore 1, Secretary.

EASTERN SECTION, AMERICAN CONGRESS OF PHYSICAL MEDICINE AND REHABILITATION, Hotel Adelphia, Philadelphia, April 7. Dr. Harold Lefkoe, 1006 Medical Tower, Philadelphia 3, Secretary.

FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, Chalfonte-Haddon Hall, Atlantic City, N. J., Apr. 16-20. Mr. M. O. Lee, 2101 Constitution Ave., Washington 25, D. C., Secretary.

HAWAII MEDICAL ASSOCIATION, Reef Hotel, Honolulu, Apr. 22-29. Dr. William S. Ito, 510 S. Beretania St., Honolulu, Secretary.

INDUSTRIAL MEDICAL ASSOCIATION, Philadelphia, Apr. 23-26. Dr. H. Glenn Gardiner, Inland Steel Co., East Chicago, Ind., Secretary.

INTERNATIONAL ACADEMY OF PROCTOLOGY, Drake Hotel, Chicago, Apr. 23-26. Dr. Alfred J. Cantor, 43-55 Kissena Blvd., Flushing, N. Y., Secretary.

INTERSTATE ORTHOPEDIC SOCIETY, Pittsburgh, April 18. Dr. Harold H. Sankey, 121 University Place, Pittsburgh 13, Secretary.

IOWA STATE MEDICAL SOCIETY, Savery Hotel and Veterans Memorial Auditorium, Des Moines, Apr. 22-25. Mr. Donald L. Taylor, 529 36th St., Des Moines 12, Executive Secretary.

JOHN A. ANDREW CLINICAL SOCIETY, Memorial Hospital, Tuskegee Institute, Alabama, Apr. 8-13. Dr. Eugene H. Dibble Jr., John A. Andrew Memorial Hospital, Tuskegee Institute, Ala., Secretary.

KANSAS MEDICAL SOCIETY, Jayhawk Hotel, Topeka, April 29-May 3. Mr. Oliver E. Ebel, 315 West 4th St., Topeka, Executive Secretary.

LOUISIANA STATE MEDICAL SOCIETY, Hotel Bentley, Alexandria, Apr. 23-25. Dr. C. Grenes Cole, 1430 Tulane Ave., New Orleans 12, Secretary.

MARYLAND, MEDICAL AND CHIRURGICAL FACULTY OF THE STATE OF, BALTIMORE, May 2-4. Dr. Everett S. Diggs, 1211 Cathedral St., Baltimore 1, Secretary.

MICROCIRCULATORY CONFERENCE, Hotel Schroeder, Milwaukee, Apr. 3. Dr. George P. Fulton, Boston University, College of Liberal Arts, 725 Commonwealth Ave., Boston 15, Chairman.

MISSOURI STATE MEDICAL ASSOCIATION, Hotel Jefferson, St. Louis, Apr. 8-11. Dr. E. Royse Bohrer, 634 North Grand Blvd., St. Louis 3, Secretary.

NATIONAL MULTIPLE SCLEROSIS SOCIETY, New York, March 13. Mr. Sidney L. Smith, Suite 7 G, 270 Park Ave., New York 17, Secretary.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS, Palmer House, Chicago, Mar. 26-28. Dr. Franklin M. Foote, 1790 Broadway, New York 19, Executive Director.

NEW MEXICO MEDICAL SOCIETY, Roswell Senior High School, Roswell, May 2-4. Mr. Ralph R. Marshall, 221 West Central Ave., Albuquerque, Secretary.

NORTH CAROLINA, MEDICAL SOCIETY OF THE STATE OF, Hotel Carolina, Pinehurst, April 30-May 2. Dr. Millard D. Hill, 203 Capitol Bldg., Raleigh, Secretary.

OHIO STATE MEDICAL ASSOCIATION, Cleveland, Apr. 10-13. Mr. Charles S. Nelson, 79 East State St., Columbus 15, Executive Secretary.

REGIONAL MEETINGS:

AMERICAN COLLEGE OF PHYSICIANS:

Southern Illinois, Springfield, March 24. Dr. Charles H. Drenckhahn, 602 West University Ave., Urbana, Governor.

AMERICAN COLLEGE OF SURGEONS:

Little Rock, Ark., Hotel Marion, March 12-13. Dr. Joseph F. Shuffield, 103 East 7th St., Little Rock, Ark., Chairman.

Edmonton, Alberta, Canada, The Macdonald, Apr. 23-25. Dr. J. Rose Vant, 10113, 104th St., Edmonton, Alberta, Canada, Chairman.

U. S. SECTION, INTERNATIONAL COLLEGE OF SURGEONS:

San Jose, Calif., St. Claire Hotel, March 22-23. Dr. Charles Mathe, 450 Sutter St., San Francisco 8, Chairman.

Madison, Wis., Loraine Hotel, April 26-28. Dr. Arnold S. Jackson, Jackson Clinic, Madison, Wis., Chairman.

Chattanooga, Tenn., Read House, April 30-May 1. Dr. William G. Stephenson, 546 McCallie Ave., Chattanooga 3, Tenn., Chairman.

RHODE ISLAND MEDICAL SOCIETY, Rhode Island Medical Society Library, Providence, May 1-3. Dr. Thomas Perry Jr., 106 Francis St., Providence 3, Secretary.

SOCIETY OF BIOLOGICAL PSYCHIATRY, Morrison Hotel, Chicago, Apr. 28-29. Dr. George N. Thompson, 2010 Wilshire Blvd., Los Angeles 5, Secretary.

SOUTHEASTERN SECTION, AMERICAN UROLOGICAL ASSOCIATION, Hollywood, Fla., Mar. 25-29. Dr. Robert F. Sharp, 200 Carondelet St., New Orleans 12, Secretary.

SOUTHEASTERN SURGICAL CONGRESS, John Marshall Hotel, Richmond, Va., Mar. 12-15. Dr. Benjamin T. Beasley, 701 Hurt Bldg., Atlanta 3, Ga., Secretary.

SOUTHERN NEUROSURGICAL SOCIETY, George Washington Hotel, Jacksonville, Fla., Mar. 23-24. Dr. William F. Meacham, Vanderbilt University Hospital, Nashville 5, Tenn., Secretary.

SOUTHWESTERN SURGICAL CONGRESS, Pioneer Hotel, Tucson, Ariz., Apr. 16-18. Dr. C. M. O'Leary, 207 Plaza Court Bldg., Oklahoma City, Secretary.

STUDENT AMERICAN MEDICAL ASSOCIATION, Hotel Sherman, Chicago, May 4-6. Mr. Russell F. Staudacher, 510 North Dearborn St., Chicago 10, Executive Secretary.

SYMPOSIUM ON FUNDAMENTAL CANCER RESEARCH, Texas Medical Center, Houston, Texas, Mar. 29-31. Dr. Grant Taylor, University of Texas, Postgraduate School of Medicine, Houston, Texas, General Chairman.

SYMPOSIUM ON PEDIATRICS, Salt Lake City, Apr. 12-13. Dr. F. Willis Taylor, 1265 West 4th North, Salt Lake City 16, Chairman.

TENNESSEE STATE MEDICAL ASSOCIATION, Peabody Hotel, Memphis, Apr. 8-11. Dr. R. H. Kampmeier, 112 Louise Ave., Nashville 5, Secretary.

TEXAS MEDICAL ASSOCIATION, Galveston, Apr. 21-25. Mr. C. Lincoln Williston, 1801 N. Lamar Blvd., Austin, Executive Secretary.

THE CONSTANTINIAN SOCIETY, Del Monte Lodge, Pebble Beach, Calif., Apr. 11-14. Dr. C. F. Shook, P. O. Box 1035-36, Toledo 1, Ohio, Secretary.

UNITED STATES-MEXICO BORDER PUBLIC HEALTH ASSOCIATION, Mexicali, Baja Calif., and Calexico, Calif., Apr. 13-16. Dr. Sidney B. Clark, 204 U. S. Court House, El Paso, Texas, Secretary.

WESTERN INDUSTRIAL MEDICAL ASSOCIATION, Hotel Ambassador, Los Angeles, Apr. 28. Dr. Edward J. Zaik, 740 S. Olive St., Room 220, Los Angeles 14, Secretary.

WESTERN SECTION, AMERICAN UROLOGICAL ASSOCIATION, Sheraton-Palace Hotel, San Francisco, April 30-May 3. Dr. James Ownby Jr., 516 Sutter St., San Francisco, Chairman.

WISCONSIN, STATE MEDICAL SOCIETY OF, Hotel Schroeder, Milwaukee, May 1-3. Mr. Charles H. Crownhart, 330 East Lakeside St., Madison 1, Secretary.

FOREIGN AND INTERNATIONAL

ASSOCIATION OF INDUSTRIAL MEDICAL OFFICERS, London School of Hygiene and Tropical Medicine, London W.C.1, England, Sept. 24-28, 1956. Dr. J. A. A. Mekelburg, Peek, Frean and Company, Ltd., Keetons Rd., Bermondsey, London, S.E.16, England, Honorable Secretary.

BRITISH MEDICAL ASSOCIATION, Brighton, England, July 9-13, 1956. Dr Angus Macrae, B. M. A. House, Tavistock Square, London, W.C.1, England.

CANADIAN MEDICAL ASSOCIATION, Quebec, P. Q., Canada, June 10-14, 1956. Dr. Arthur D. Kelly, 150 St. George St., Toronto 5, Ont., Canada, Secretary.

CONFERENCE OF INTERNATIONAL UNION FOR HEALTH EDUCATION OF THE PUBLIC, Rome, Italy, April 27-May 5, 1956. Mr. Lucien Viborel, 92 rue St. Denis, Paris 1er, France, Secretary-General.

CONGRESS OF FRENCH SOCIETY OF OPHTHALMOLOGY, Paris, France, May 6-10, 1956. Dr. Marcel Kalt, 81 rue Saint-Lazare, Paris 9e, France, Secretary.

CONGRESS OF INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, Miami Beach, Fla., U.S.A., April 9-12, 1956. For information write: Mrs. L. McMechan, 318 Hotel West Lake, Rocky River, Ohio, U. S. A.

CONGRESS OF INTERNATIONAL ASSOCIATION OF LIMNOLOGY, Helsinki, Finland, July 26-Aug. 7, 1956. For information address: Dr. H. Luther, Snellmansgatan 16 C 36, Helsinki, Finland.

CONGRESS OF INTERNATIONAL ASSOCIATION OF LOGOPEDICS AND PHONIATRICS, Barcelona, Spain, Sept. 3-7, 1956. Dr. J. Perello, Provenza 319, Barcelona 9, Spain, Secretary-General.

CONGRESS OF INTERNATIONAL SOCIETY OF HEMATOLOGY, Hotel Somerset, Boston, Mass., U.S.A., Aug. 27-Sept. 1, 1956. Dr. W. C. Moloney, 39 Bay State Road, Boston, Mass., U.S.A., Secretary.

CONGRESS OF INTERNATIONAL UNION AGAINST TUBERCULOSIS, New Delhi, India, Jan. 3-6, 1957. For information address: Secretariat, The Union, 66 Boulevard Saint-Michel, Paris 6e, France.

CONGRESS OF LATIN SOCIETY OF OPHTHALMOLOGY, Madrid, Spain, April 24-28, 1956. For information address: Dr. Costi, Montalban 3, Madrid, Spain.

EUROPEAN CONGRESS OF ALLERGOLOGY, Florence, Italy, Sept. 12-15, 1956. Prof. Umberto Serafini, Instituto de Patologia Medica, Viale Morgagni, Florence, Italy, Secretary-General.

EUROPEAN CONGRESS OF CARDIOLOGY, Stockholm, Sweden, Sept. 10-14, 1956. Dr. Karl Erik Grewin, Sodersjukhuset, Stockholm, Sweden, General Secretary.

EUROPEAN SYMPOSIUM ON VITAMIN B_{12}, Hamburg, Germany, May 22-26, 1956. For information write: Doz. Dr. H. Bauer, Nervenklinik, Hamburg-Eppendorf, Germany.

HEALTH CONGRESS, ROYAL SOCIETY FOR THE PROMOTION OF HEALTH, Blackpool, England, April 24-27, 1956. Mr. P. Arthur Wells, 90 Buckingham Palace Road, London S.W. 1, England, Secretary.

INTER-AMERICAN CONGRESS OF CARDIOLOGY, Havana, Cuba, Nov. 4-10, 1956. For information address: Dr. Ramon Aixala, Apartado 2108, Havana, Cuba.

INTERNATIONAL ACADEMY OF PATHOLOGY, Cincinnati, Ohio, U. S. A., April 24-25, 1956. Dr. F. K. Mostofi, Armed Forces Institute of Pathology, Washington 25, D. C., U. S. A., Secretary.

INTERNATIONAL CONGRESS AGAINST ALCOHOLISM, Istanbul, Turkey, Sept. 10-15, 1956. For information address: International contre l'Alcoolisme, Case Gare 49, Lausanne, Switzerland.

INTERNATIONAL CONGRESS ON ANIMAL REPRODUCTION, Arts School, University of Cambridge, Cambridge, England, June 25-30, 1956. Dr. Joseph Edwards, Production Division, Milk Marketing Board, Thames Ditton, Surrey, England, Hon. Secretary.

INTERNATIONAL CONGRESS OF ANTHROPOLOGICAL AND ETHNOLOGICAL SCIENCES, Philadelphia, Pa., U. S. A., Sept. 2-9, 1956. Dr. William N. Fenton, National Research Council, Division of Anthropology and Psychology, 2101 Constitution Avenue, Washington 25, D. C., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF DIETETICS, Congress Palace, Esposizione Universale Roma, Rome, Italy, Sept. 10-14, 1956. Prof. E. Serianni, Associazione Dietetica, Italiana, via dei Penitenzieri N. 13, Rome, Italy, Secretary General.

INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST, Cologne, Germany, Aug. 19-23, 1956. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Illinois, U. S. A., Executive Director.

INTERNATIONAL CONGRESS OF ENTOMOLOGY, Montreal, Canada, Aug. 17-25, 1956. Mr. J. A. Downes, Science Service Bldg., Carling Ave., Ottawa, Ont., Canada, Secretary.

INTERNATIONAL CONGRESS OF GASTROENTEROLOGY, London, England, July 18-21, 1956. Mr. Hermon Taylor, London Hospital, White Chapel, London E.1, England, Honorable Secretary.

INTERNATIONAL CONGRESS OF HEALTH TECHNICIANS, Maison de la Mutualite, Paris, France, June 5-8, 1956. For information address: Mr. M. H. Thoillier, 37 Rue de Monthlon, Paris 9e, France.

INTERNATIONAL CONGRESS FOR THE HISTORY OF SCIENCE, Florence and Milan, Italy, Sept. 3-10, 1956. Dr. M. L. Bonelli, Instituto di Ottica, Arcetri, Florence, Italy, Secretary-General.

INTERNATIONAL CONGRESS OF HUMAN GENETICS, Copenhagen, Denmark, Aug. 1-6, 1956. For information address: The University Institute for Human Genetics, Tagensvej 14, Copenhagen N, Denmark.

INTERNATIONAL CONGRESS OF HYDATID DISEASE, Athens, Greece, Sept. 14-18, 1956. Prof. B. Kourias, Croix-Rouge Hellenique, 1 rue Mackenzie King, Athens, Greece, Secretary-General.

CHICAGO MEDICAL LIBRARY

INTERNATIONAL CONGRESS ON INFECTIOUS PATHOLOGY, Lyon, France, May 24-26, 1956. General Secretariat: Institut Pasteur de Lyon, 77 rue Pasteur, Lyon, France.

INTERNATIONAL CONGRESS OF INTERNAL MEDICINE, Madrid, Spain, Sept. 19-23, 1956. Dr. J. C. De Oya and Dr. J. Gimena, Hostaleza No. 90, Madrid, Spain, Secretaries.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, Palmer House, Chicago, Illinois, U. S. A., Sept. 9-13, 1956. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U. S. A., Secretary-General.

INTERNATIONAL CONGRESS ON MEDICAL RECORDS, Shoreham Hotel, Washington, D. C., U. S. A., Oct. 1-5, 1956. For information address: Miss Doris Gleason, Executive Director, American Association of Medical Record Librarians, 510 North Dearborn St., Chicago 10, Illinois, U. S. A.

INTERNATIONAL CONGRESS OF NEO-HIPPOCRATIC MEDICINE, Montecatini, Terme, Italy, May 20-22, 1956. Dr. Valente, 41 Avenue Verdi, Montecatini Terme, Italy, Secretary-General.

INTERNATIONAL CONGRESS OF PAEDIATRICS, Copenhagen, Denmark, July 22-27, 1956. Professor P. Plum, Rigshospitalet, Copenhagen, Denmark, President.

INTERNATIONAL CONGRESS OF PHYSICAL MEDICINE, Copenhagen, Denmark, August 20-24, 1956. Dr. B. Strandberg, Kobenhavns amts sygehus i Gentofte, Dept. of Rheumatology and Physical Medicine, Hellerup, Denmark, Honorable Secretary.

INTERNATIONAL CONGRESS OF RADIOLOGY, Mexico, D. F., Mexico, July 22-28, 1956. Dr. Jose Noriega, Tepic 126 (2e piso), Mexico, D. F. 7, Mexico, Secretary General.

INTERNATIONAL CONGRESS OF WORLD CONFEDERATION FOR PHYSICAL THERAPY, Hotel Statler, New York, New York, U. S. A., June 17-23, 1956. For information address: Miss Mildred Elson, American Physical Therapy Association, 1790 Broadway, New York 19, New York, U. S. A.

INTERNATIONAL GENETICS SYMPOSIUM, Tokyo and Kyoto, Japan, Sept. 6-12, 1956. For information address: Secretary, International Genetics Symposium, Science Council of Japan, Ueno Park, Tokyo, Japan.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Brussels, Belgium, July 29-Aug. 5, 1956. For information address: Prof. J. Reuse, Faculte de Medicine et de Pharmacie, 115 Boulevard de Waterloo, Brussels, Belgium.

INTERNATIONAL PROFESSIONAL UNION OF GYNECOLOGISTS AND OBSTETRICIANS, Madrid, Spain, Sept. 28-29, 1956. Dr. Jacques Courtois, 1 rue Racine, St-Germain-en-Laye (S and O), France, Permanent International Secretary-General.

INTERNATIONAL SYMPOSIUM ON DIENCEFALON, Musec della Scienza e della Tecnica, Piazza S. Vittorre 21, Milan, Italy, May 3-5, 1956. Drs. S. Curri and L. Martini, Instituto di Farmacologia, Universita di Milano, via Andre del Sarto 21, Milan, Italy, Secretaries.

INTERNATIONAL SYMPOSIUM ON VENEREAL DISEASES AND THE TREPONEMATOSES, Hotel Statler, Washington, D. C., U. S. A., May 28-June 1, 1956. For information address: Dr. Charles A. Smith, Chief, Venereal Disease Program, Division of Special Health Services, Public Health Service, Dept. of Health, Education and Welfare, Washington 25, D. C., U. S. A.

LATIN AMERICAN CHAPTER, INTERNATIONAL SOCIETY OF ANGIOLOGY, Havana, Cuba, Nov. 8-11, 1956. Dr. Armando Nuñez Nuñez, 25 No. 510 Vedado, Havana, Cuba, President.

MEDICAL WOMEN'S INTERNATIONAL ASSOCIATION, EXTRAORDINARY GENERAL ASSEMBLY, Burgenstock, Nidwalden, Switzerland, Sept. 21-24, 1956. Dr. Janet Aitken, 30a Acacia Road, London N.W. 1, England, Secretary.

MIDDLE EAST MEDICAL ASSEMBLY, Campus, American University of Beirut, Beirut, Lebanon, April 7-9, 1956. Dr. Virgil C. Scott, American University of Beirut, Beirut, Lebanon, Chairman.

NATIONAL CONGRESS OF PEDIATRICS, Cuidad Universitaria, Mexico D.F., Mexico, May 1-5, 1956. Dr. Ignacio Avila Cisneros, Calzada de Madereros No. 240, Mexico 18, D.F., Mexico, Coordinator.

NORTH QUEENSLAND MEDICAL CONFERENCE, Cairns, North Queensland, Australia, June 25-30, 1956. Dr. W. R. Horsfall, P. O Box 672, Cairns, N.Q., Australia, Secretary.

PAKISTAN MEDICAL CONFERENCE, University of Peshawar, Peshawar, Pakistan, Apr. 2-4, 1956. Dr. M. W. Alivi, 9, Braganza House, Napier St., Saddar, Karachi, Pakistan, Secretary General.

PAN AMERICAN CONGRESS ON CANCER CYTOLOGY, Miami, Fla., U. S. A., Jan. 8-12, 1957. Dr. J. Ernest Ayre, 1155 N.W. 14th St., Miami, Fla., U. S. A., General Chairman.

PAN AMERICAN CONGRESS OF GERONTOLOGY, Mexico, D. F., Mexico, Sept. 5-15, 1956. Dr. Manuel Payno, Avenue Cuahtemoc No. 10-3, Mexico 7, D. F., Mexico, Presidente.

PAN AMERICAN CONGRESS OF OTORHINOLARYNGOLOGY AND BRONCHOESOPHAGOLOGY, San Juan, Puerto Rico, April 8-12, 1956. Dr. C. E. Munoz MacCormick, Apartado 9111, Santurce 29, Puerto Rico, Secretary General.

PAN AMERICAN TUBERCULOSIS CONGRESS, Medellin and Bogota, Columbia, South America, Aug. 1-15, 1956. General Secretary, 26 de Marzo 1065, Montevideo, Uruguay.

WORLD CONGRESS ON FERTILITY AND STERILITY, Naples, Italy, May 18-24, 1956. Dr. Maxwell Roland, 114-20 Queens Boulevard, Forest Hills 75, New York, N. Y., U. S. A., Chairman, Liaison Committee.

WORLD FEDERATION FOR MENTAL HEALTH, Munich, Germany, Aug. 12-18, 1956. Secretariat, 19 Manchester Street, London W.1, England.

WORLD MEDICAL ASSOCIATION, Havana, Cuba, Oct. 9-15, 1956. Dr. Louis H. Bauer, 345 East 46th St., New York 17, New York, U. S. A., Secretary-General.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Various Centers. April 24-25 (Part II); June 19-20 (Parts I and II); September 4-5 (Part I). Candidates may file applications at any time but they must be received at least six weeks before the date of the examination for which application is made. New candidates should apply by formal registration; registered candidates may notify the board, indicating desired location, date and candidate number. Ex. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 19-21. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

ARIZONA:* *Examination.* Phoenix, April 18. *Reciprocity.* Phoenix, April 21. Exec. Sec., Mr. Robert Carpenter, 541 Security Bldg., Phoenix.

ARKANSAS:* *Examination.* Little Rock, June 14-15. Sec., Dr. Joe Verser, Harrisburg.

COLORADO:* *Endorsement.* Denver, April 10. Final date for filing application is March 12. *Examination.* Denver, June 12-13. Exec. Sec., Miss Beulah H. Hudgens, 831 Republic Bldg., Denver 2.

CONNECTICUT:* *Examination.* New Haven, March 12-14. Sec., Dr. Creighton Barker, 160 St. Ronan St., New Haven.

DELAWARE: *Examination.* Dover, July 10-12. *Reciprocity.* Dover, July 19. Sec., Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA:* *Examination.* Washington, May 14-15. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N.W., Washington.

FLORIDA:* *Examination.* Miami Beach, June 24-26. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

GEORGIA: *Examination and Reciprocity.* Atlanta, June. Sec., Mr. Cecil L. Clifton, 111 State Capitol, Atlanta 3.

IDAHO: *Examination, Reciprocity and Endorsement.* Boise, July 9-11. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

ILLINOIS: *Examination and Reciprocity.* Chicago, April 3-5, June 19-21 and Oct. 9-11. Supt. of Regis., Mr. Frederic B. Selcke, Capitol Building, Springfield.

INDIANA: *Examination.* Indianapolis, June. Exec. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

IOWA:* *Reciprocity.* Des Moines, April 23. *Examination.* Iowa City, June 11-13. Exec. Sec., Mr. Ronald V. Saf, 310 Bankers Trust Bldg., Des Moines.

KANSAS: *Examination and Reciprocity.* Kansas City, June 6-7. Sec., Dr. Lyle F. Schmaus, 872 New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, June 4-6. Sec., Dr. Russell E. Teague, 620 S. Third St., Louisville 2.

LOUISIANA: *Homeopathic.* Subject to call. Sec., Dr. F. H. Hardenstein, 903 Pere Marquette Bldg., New Orleans 12.

MAINE: *Examination.* Portland, Mar. 13-14. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Examination.* Baltimore, June 19-20. Sec., Dr. Lewis P. Gundry, 1211 Cathedral St., Baltimore.

MARYLAND: *Homeopathic. Reciprocity.* Havre de Grace, April 5. *Examination,* Havre de Grace, June 25-27. Sec., Dr. Robert H. Reddick, R.D. #2, Cambridge.

MASSACHUSETTS: *Examination.* Boston, July 10-13. Sec., Dr. Robert C. Cochrane, Room 37, State House, Boston.

MICHIGAN:* *Examination.* Ann Arbor and Detroit, June 13-15. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., Lansing.

MINNESOTA:* *Examination and Reciprocity.* Minneapolis, June 12-14. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: *Examination.* Jackson, June 25-26. *Reciprocity.* Jackson, June 27. Asst. Sec., Dr. R. N. Whitfield, Old Capitol, Jackson.

MONTANA: *Examination and Reciprocity.* Helena, April 3. Sec., Dr. S. A. Cooney, 7 West 6th Ave., Helena.

NEBRASKA:* *Examination.* Omaha, June 18-20. Director, Bureau of Examining Boards, Mr. Husted K. Watson, 1009 State Capitol Bldg., Lincoln.

NEVADA: *Examination and Reciprocity.* Reno, April 3. Sec., Dr. G. H. Ross, 112 Curry St., Carson City.

NEW HAMPSHIRE: *Examination and Endorsement.* Concord, March 14-16. Sec., Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 19-22. Sec., Dr. Patrick H. Corrigan, 28 W. State St., Trenton.

NEW MEXICO:* *Examination and Endorsement.* Santa Fe, May 21-22. Sec., Dr. R. C. Derbyshire, 227 E. Palace Ave., Santa Fe.

NORTH CAROLINA: *Endorsement.* Pinehurst, April 30. *Examination.* Raleigh, June 18-21. Sec., Dr. Joseph J. Combs, Professional Bldg., Raleigh.

NORTH DAKOTA: *Examination.* Grand Forks, July 11-13. *Reciprocity and Endorsement.* Grand Forks, July 14. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Examination.* Columbus, June 14-16. *Endorsement.* Columbus, April 3. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus.

OKLAHOMA:* *Examination.* Oklahoma City, June 5-6. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Reciprocity*. Portland, Apr. 19-21. *Examination*. Portland, July. Ex. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland.
PENNSYLVANIA: *Examination*. Philadelphia and Pittsburgh, July 9-12. Acting Sec., Mrs. Margaret G. Steiner, Box 911, Harrisburg.
RHODE ISLAND:* *Endorsement*. Providence, March 29. *Examination*. Providence, April 5-6. Admin. of Prof. Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.
SOUTH CAROLINA: *Reciprocity*. Myrtle Beach, May 15. *Examination*. Columbia, June 25-26. Sec., Mr. N. B. Heyward, 1329 Blanding St., Columbia.
SOUTH DAKOTA:* *Examination*. Custer, July 17-19. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.
TENNESSEE:* *Examination*. Memphis, March 28-29. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.
TEXAS:* *Examination and Reciprocity*. Fort Worth, June 18-20. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.
UTAH: *Examination*. Salt Lake City, July 11-13. Director, Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.
VIRGINIA: *Reciprocity*. Richmond, June 13. *Examination*. Richmond, June 14-16. Address, Board of Medical Examiners, 631 First St., S.W., Roanoke.
WASHINGTON:* *Endorsement*. Seattle, July 15. *Examination*. Seattle, July 16-18. Sec., Mr. Edward C. Dohm, Olympia.
WEST VIRGINIA: *Examination*. Charleston, July. *Reciprocity*. Charleston, April 23. SEC., Dr. N. H. Dyer, State Office Bldg. No. 3, Charleston.
WISCONSIN:* *Reciprocity*, Madison, Spring; *Reciprocity and Examination*. Milwaukee, July 10-12. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., Madison.
WYOMING: *Examination and Reciprocity*. Cheyenne, June 4. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.
ALASKA:* On application in Anchorage, Fairbanks, Juneau and other towns. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.
GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Sec., Dr. John E. Kennedy, Agana.
VIRGIN ISLANDS: *Examination and Endorsement*. Charlotte Amalie, June 13-14. Sec., Dr. Earle M. Rice, St. Thomas.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARIZONA: *Examination and Reciprocity*. Tucson, March 20. Sec., Dr. H. D. Rhodes, University of Arizona, Tucson.
ARKANSAS: *Examination*. Little Rock, May 4-5. Sec., Mr. S. C. Dellinger, Zoology Department, University of Arkansas, Fayetteville.
COLORADO: *Examination and Reciprocity*. Denver, May 2-3. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.
DISTRICT OF COLUMBIA: *Examination*. Washington, April 23-24. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave. N.W., Washington 6.
FLORIDA: *Examination*. Miami, June 9. Sec., Mr. M. W. Emmel, Box 340, Gainesville.
IOWA: *Examination and Reciprocity*. Des Moines, April 10. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.
MINNESOTA: *Examination*. Minneapolis, April 3-4. Sec., Dr. Raymond M. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis 14.
NEVADA: *Examination*. Reno, April 3. Sec., Dr. Donald G. Cooney, Box 9005, University Station, Reno.
OKLAHOMA: *Examination and Reciprocity*. Oklahoma City, Mar. 30-31. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.
OREGON: *Examination*. Portland, March 3; June 2, Sept. 8 and Dec. 1. Dr. Earl M. Pallett, Sec., State Board of Higher Education, Eugene.
TENNESSEE: *Examination*. Memphis, Mar. 21-22. Sec., Mr. O. W. Hyman, 62 S. Dunlap St., Memphis 3.
TEXAS: *Examination*. Austin, Galveston and Huston, April 13-14. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.
WASHINGTON: *Reciprocity*. Seattle, July 10. *Examination*. Seattle, July 11-12. Sec., Mr. Edward C. Dohm, Olympia.
WISCONSIN: *Examination*. Madison, April 7 and Milwaukee, June 2. Final date for filing application is Mar. 30. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.
ALASKA: *Examination and Reciprocity*. Anchorage and Juneau, first week of February, April, June, August and November. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

*Basic Science Certificate required.

MAGAZINE–TELEVISION REPORT

The following list of current medical articles in mass-circulation magazines and forthcoming network television programs on medical subjects is published each week only for the information of readers of THE JOURNAL. *Unless specifically stated, the American Medical Association neither approves nor disapproves of the articles and programs reported.*

TELEVISION

Sunday, March 18

CBS-TV, 5 p. m. EST. "Out of Darkness," a 90-minute documentary on mental health, filmed primarily in the Metropolitan State Hospital, Norwalk, Calif. Dr. William C. Menninger will be the medical narrator.

Monday, March 19

NBC-TV, 11 a. m.-noon EST. "Medical and Health News with Howard Whitman," a segment of the "Home" show.

NBC-TV, 9 p. m. EST. "Medic" takes up the subject of infant blindness in a teleplay titled "My Best Friend, My Guilty Friend."

MAGAZINES

Saturday Evening Post, Feb. 25, 1956

"Who Cares About Us?"

"The question of how to protect children from injury—both physical and emotional—at the hands of a psychotic parent is one which must be considered as a part of our mental health problem." A mother reports on her attempts to provide hard-to-get psychiatric help for her mentally ill husband.

Family Weekly Magazine, March 4, 1956

"Let's Cure Drug Addicts, Not Punish Them!" by Dr. Hubert S. Howe, as told to Jerry Klein

Speaking for the New York Academy of Medicine's drug-addiction subcommittee, of which he is chairman, the author recommends a national system of clinics "which would provide drugs to addicts free or at low cost as long as these unfortunates let doctors try to cure and rehabilitate them."

Saturday Evening Post, March 10, 1956

"The Doctor Who Sticks His Neck Out," by Greer Williams

According to the subtitle: "Dr. Elmer Hess, outspoken head of the American Medical Association, doesn't believe in reticence about anything, not even his own fees. A portrait of the medical world's mouthpiece."

American Magazine, March, 1956

"The Case for Standard Doctors' Fees," by Edward J. McCormick, M.D.

A former president of the American Medical Association says "the traditional system of computing fees requires radical change and improvements, not only for the protection of the public, but for the sake of the honest and conscientious physicians who make up the great bulk of the profession." He recommends that "doctors establish schedules of average fees for common medical services on a local basis and make these fees known to the public."

Parade, March 11, 1956

"A Woman's 12-Day Ordeal with Cancer," by Robert P. Goldman

"A documentary, inside-the-hospital report of the tension, drama—and hope—of a cancer operation." Photographed during a 12-day period at New York University-Bellevue Medical Center.

Better Homes and Gardens, March, 1956

"Your Child's Health: What About House Calls," by Francis Kodl, M.D.

The author points out that the trend is away from house calls, except in emergencies, since a doctor can do a better job in his office and can better allocate his time. However, if it is necessary to call a doctor, he says "it is important for you to know how you can get more from your doctor's visit."

Ladies' Home Journal, March, 1956

"The Difference Between Life and Death—'Frontier' Blood Bank," by Margaret Hickey

Volunteers who operate the Red Cross blood program in Montana collect, and supply to 42 participating hospitals, the 14,500 pt. of blood needed in an average year.

GOVERNMENT SERVICES

ARMY

Six New Consultant Committees to Assist Army.—Six committees on civilian consultants to army surgeons in the zone of the interior have been formed by the surgeon general, in cooperation with the society of medical consultants to the armed forces. The committees, which have a membership of at least three outstanding physicians in the area, represent the fields of medicine, surgery, and neuropsychiatry. They will be called on to assist the army surgeon in the professional appraisal, procurement, and appointment of professional consultants to local medical installations; in the supervision of civilian medical consultation in class 1 Army medical installations; and in other matters pertaining to the maintenance of the highest standards of professional performance within the command. Committee chairmen in each of the Army areas are: first Army, Bruce Webster, M.D., New York; second Army, I. S. Ravdin, M.D., Philadelphia; third Army, Joseph S. Skobba, M.D., Atlanta, Ga.; fourth Army, Perry C. Talkington, M.D., Dallas, Texas; fifth Army, James B. Mason, M.D., Chicago; sixth Army, Manfred U. Prescott, M.D., San Francisco, Calif.

NAVY

Medical Officer Commended.—Lieut. Commander Paul D. Doolan, M. C., chief, research division and metabolic research facility at the Naval Hospital, Oakland, has been commended by the surgeon general for his work in that capacity. The surgeon general's letter, in part, stated that the accomplishments under Dr. Doolan's direction have been a source of pride to the entire Navy medical department and concluded with the statement, "You have applied yourself to your duties well beyond the normal requirement of time, energy, and enthusiasm."

Dr. Doolan's work with the Navy's artificial kidney has attracted wide attention in the San Francisco Bay area. He has been on active duty in the Medical Corps since 1948. He is certified by the American Board of Internal Medicine. Dr. Doolan is also a certified Navy boxing coach.

Meeting of Joint Committee on Aviation Pathology.—The Armed Forces Institute of Pathology was host to the first formal meeting of a Department of Defense–sponsored joint committee on aviation pathology, on Feb. 7. Medical officers from the three U. S. armed services were joined by observers from the United Kingdom and Canada as the groundwork was laid for an organization interested in pathology as applied to aviation and flight safety. The group will collect information on the correlation between pathological evidence and causative factors of jet aircraft accidents.

"Navy Log" Filmed.—The physical therapy service of the Naval Hospital, Oakland, Calif., during the week of Jan. 23 was temporarily transformed into a movie studio, where CBS filmed sequences for "Navy Log," a CBS television show. The film titled, "Not a Leg to Stand on," the story of an amputee at Oak Knoll, is to be aired sometime in June.

"Navy Log," which telecasts each Tuesday at 8:30 p. m. over CBS, is transmitted over 130 stations to an audience of about 20 million.

Retirement of Officers.—The following medical department officers were transferred to the retired list of the Navy on Feb. 1, 1956. Nondisability retirements: Rear Adm. David C. Gaede, M. C., U. S. N. (retired in next higher grade than that in which serving, by reason of a combat citation), and Capt. Dirk M. te Groen, M. C., U. S. N. Physical disability retirements: Lieut. Commander George H. Powers, M. C., U. S. N. R., and Lieut. (j. g.) Bruce C. Jeppson, M. C., U. S. N. R.

VETERANS ADMINISTRATION

Veterans Hospital Completed During 1955.—The 1,000 bed neuropsychiatric hospital at Sepulveda, Calif., in the San Fernando Valley, illustrated on this page, was the only Veterans Administration Hospital completed during the calendar year of 1955. This one made a total of 61 new hospitals constructed in recent years, including the hospitals at Lebanon, Pa., and Tomah, Wis. As of Dec. 31, construction of five other new hospitals was in progress. The construction contract had been awarded for one hospital, the design was in progress in two, and the design had not been started in two. The total number of sites that had then been acquired for new hospitals was 67, while one other hospital site had been approved but not yet acquired. Illustrations of new veterans' hospitals completed during several previous calendar years were published in THE JOURNAL, May 6, 1950, page 123; March 10, 1951, page 748; March 1, 1952, page 760; May 2, 1953, page 69; May 1, 1954, page 58; and March 5, 1955, page 845.

The total veteran population in civil life on Dec. 31 was 22,131,000 (a preliminary figure subject to revision). The total average daily hospital care load for veterans of all wars was 111,195, of whom 2,901 were in non-VA hospitals. The average daily load of veterans of all wars in domiciliary care was 17,100.

VA hospital in Sepulveda, Calif.

PUBLIC HEALTH SERVICE

Announcement of Regular Corps Examinations for Medical Officers.—A competitive examination for appointment of medical officers to the regular corps of the United States Public Health Service will be held in various places throughout the country on June 12-15. Appointments provide opportunities for career service in clinical medicine, research, and public health. They will be made in the ranks of assistant and senior assistant, equivalent to Navy ranks of lieutenant (j. g.) and lieutenant. Entrance pay for an assistant surgeon with dependents is $6,017 per year; for senior assistant surgeon with dependents, $6,918. Qualified officers are promoted at regular intervals. Benefits other than promotions include periodic pay increases, 30 days' annual sick leave, medical care, disability retirement pay, regular retirement pay, which is three-fourths of annual basic pay at time of retirement, and other privileges. Active duty as a PHS officer fulfills the obligations of selective service.

Requirements for both ranks are U. S. citizenship, age of at least 21 years, and graduation from a recognized school of medicine. For the rank of assistant surgeon, at least seven years of collegiate and professional training and appropriate experience are needed. For senior assistant surgeon, an additional 3 years, for a total of at least 10 years of collegiate and professional training and appropriate experience, are required. Entrance examinations will include an interview, physical examination, and comprehensive objective examinations in the professional field.

Application forms may be obtained from the Chief, Division of Personnel, Public Health Service, Department of Health, Education, and Welfare, Washington 25, D. C. Completed application forms must be received in the Division of Personnel no later than April 30, 1956.

UNIVERSITY OF MICHIGAN LIBRARIES

DEATHS

Shorr, Ephraim, New York City; born in New Haven, Conn., June 1, 1897; Yale University School of Medicine, New Haven, 1922; associate professor of medicine (endocrinology) at Cornell University Medical College; specialist certified by the American Board of Internal Medicine; member of the American Society for Pharmacology and Experimental Therapy, Harvey Society, Association of American Physicians, Medical Society of the State of New York, American Society for Clinical Investigation, American Physiological Society, Association for the Study of Internal Secretions, Society for Experimental Biology and Medicine, and the American Psychosomatic Society; served during World War I; on July 14, 1950, the College of Physicians of Philadelphia awarded him the Alvarenga Prize for 1950 for outstanding work in shock treatment; formerly a fellow and research associate at the Russell Sage Institute; in 1944, a civilian consultant to the Office of Scientific Research and Development and consultant to the U. S. Public Health Service; since 1946, attending physician on the staff of the New York Hospital; died Jan. 6, aged 58, of coronary thrombosis.

Vrooman, Earle Morey ⊕ North Adams, Mass.; born in Trenton, N. Y., Nov. 12, 1877; Baltimore Medical College, 1903; veteran of the Spanish-American War; for 14 years, beginning in 1927, was medical officer of the Third Battalion, 104th Infantry Regiment, National Guard, with the rank of captain; when the National Guard was called into active federal service in December, 1941, was advanced to the rank of major and was made commanding officer of the regiment's medical detachments; served 10 months on active duty with the regiment until retired on reaching the age limit of 64 years; in May, 1942, was named medical officer of the state guard's 28th Infantry regiment; at one time was a member of the North Adams recreation commission; for many years school medical inspection officer; served as director of health and sanitation of the board of health of North Adams; on the staff of the North Adams Hospital; died Dec. 20, aged 78, of bronchopneumonia, cerebral hemorrhage, and arteriosclerosis.

Roberson, Foy, Durham, N. C.; born in Chapel Hill Sept. 9, 1884; Jefferson Medical College of Philadelphia, 1909; member of the founders group of the American Board of Surgery; past-president of the North Carolina State Board of Medical Examiners; in 1933 elected vice-president of the Tri-State Medical Association of the Carolinas and Virginia; member of the Southern Surgical Association, of which he was at one time vice-president, and the Medical Society of the State of North Carolina; fellow of the American College of Surgeons; served during World War II; at one time member of the board of directors of the state prison, and member of the city planning and zoning commission; for many years served as a trustee of the University of North Carolina and a member of its athletic council; consulting surgeon at Lincoln Hospital in Durham and at State Hospital, Raleigh; chief of the surgical staff at the Watts Hospital; member of the visiting staff of the Duke Hospital, where he died Nov. 19, aged 71.

Tobey, Harold Grant ⊕ Boston; born in Lancaster, Mass., Dec. 22, 1884; Harvard Medical School, Boston, 1911; specialist certified by the American Board of Otolaryngology; member of the American Laryngological Association, American Laryngological, Rhinological and Otological Society, and the American Otological Society; fellow of the American College of Surgeons; for many years on the faculty of his alma mater; during World War I served with the first Harvard unit in the British Expeditionary Forces and later with the Massachusetts General Hospital unit number six in France; consultant, Community Hospital, Keene, N. H., and Eastern Maine General Hospital in Bangor, Maine; on the staff of the Massachusetts Eye and Ear Infirmary, Children's Hospital, the New England Baptist Hospital, and New England Deaconess Hospital; died Dec. 26, aged 71, of ruptured abdominal aneurysm.

⊕ Indicates Member of the American Medical Association.

Vidrine, Arthur ⊕ Ville Platte, La.; born in Ville Platte Dec. 20, 1897; Tulane University of Louisiana School of Medicine, New Orleans, 1921; first dean, and professor of surgery, at the Louisiana State University School of Medicine, which he founded and organized in 1931; formerly professor of gynecology at his alma mater; member of the International College of Surgeons and the American Academy of General Practice; founded and operated his own hospital in Villa Platte until his retirement in 1950; served as superintendent of the Charity Hospital in New Orleans from 1928 to 1936; received honorary doctor of law degree from Louisiana State University in August, 1952; member of the board of directors of the Evangeline Bank and Trust Company; died in Hotel Dieu Dec. 20, aged 58, of cerebral hemorrhage, hypertension, and pneumonia.

Peters, John Punnett, New Haven, Conn.; born in Philadelphia in 1887; Columbia University College of Physicians and Surgeons, New York, 1913; John Slade Ely Professor of Medicine at Yale University School of Medicine; specialist certified by the American Board of Internal Medicine; member of the Connecticut State Medical Society, Society for Experimental Biology and Medicine, Association of American Physicians, and the American Society for Clinical Investigation; served overseas during World War I; on the staffs of the New Haven Dispensary and the Grace-New Haven Community Hospital; author of "Body Water"; joint author of "Quantitative Clinical Chemistry"; died in the Gaylord Farm Sanatorium in Wallingford Dec. 29, aged 68, of myocardial infarction.

Upham, Roy, New York City; born in Dartmouth, Mass., in 1879; New York Homeopathic Medical College and Hospital, New York City, 1901; professor of medicine at his alma mater, now the New York Medical College, Flower and Fifth Avenue Hospitals; specialist certified by the American Board of Internal Medicine; member of the American Gastroenterological Association, of which he was secretary general; fellow of the International College of Surgeons and the American College of Surgeons; gastroenterologist at the Flower and Fifth Avenue Hospitals; consulting physician, Metropolitan Hospital; consultant, Evangelical Deaconess Hospital in Brooklyn and the Jamaica (N. Y.) Hospital; died Jan. 5, aged 76, of pulmonary edema and reticulum cell sarcoma.

Felton, Lester Mahan ⊕ Worcester, Mass.; born in Worcester Dec. 24, 1896; Cornell University Medical College, New York City, 1922; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons; past-president of the Worcester District Medical Society; on the staffs of the Worcester Hahnemann, Worcester City, and Worcester State hospitals; consultant at the Veterans Administration Hospital in Rutland Height, Harrington Memorial Hospital in Southbridge, Henry Heywood Memorial Hospital in Gardner, and the Webster (Mass.) District Hospital; died in the Worcester Hahnemann Hospital Dec. 25, aged 58, of coronary thrombosis.

Hall, Frank Marion ⊕ Gainesville, Fla.; born in Gainesboro, Tenn., Sept. 12, 1902; University of Tennessee College of Medicine, Memphis, 1933; specialist certified by the American Board of Preventive Medicine; served as vice-president of the Alachua County Medical Society, secretary of the American Association of Public Health Physicians, president of the Florida Public Health Association, and president of the Southern Branch of the American Public Health Association; county health director; formerly director of the Limestone County Health Unit in Athens, Ala.; died in the Riverside Hospital, Jacksonville, Dec. 23, aged 53, of carcinoma of the prostate.

Hory, Joseph Stanton ⊕ New York City; born May 10, 1895; Fordham University School of Medicine, New York City, 1919; assistant clinical professor of ophthalmology at New York Medical College, Flower and Fifth Avenue Hospitals; specialist certified by the American Board of Ophthalmology; member of

the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; for many years on the staff of the Morrisania Hospital; on the staff of Seton and Union hospitals; formerly associated with the Bronx Eye and Ear Infirmary and the Manhattan Eye, Ear and Throat Hospital; died Jan. 1, aged 60, in a fire that destroyed his apartment.

Rutherford, Thomas Arthur, Carbondale, Pa.; born in 1880; University of Pennsylvania Department of Medicine, Philadelphia, 1907; specialist certified by the American Board of Psychiatry and Neurology; fellow of the American Psychiatric Association; a charter member and past-president of the Pennsylvania Psychiatric Society; served as superintendent of the Farview State Hospital in Waymart and the Hillside Home and Hospital for Mental Diseases at Clarks Summit, now known as the Clarks Summit State Hospital; died in the Carbondale (Pa.) Hospital Dec. 22, aged 75, of adenocarcinoma.

Thompson, Samuel Evans ✠ Kerrville, Texas; born May 24, 1871; Kentucky School of Medicine, Louisville, 1904; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the House of Delegates of the American Medical Association from 1934 to 1936, 1938-1939, and from 1941 through 1943; past-president of the State Medical Association of Texas; for many years medical superintendent of the Thompson Sanatorium, which he owned; consultant at the Sid Peterson Memorial Hospital; died Jan. 12, aged 84, of arteriosclerosis.

Gloyne, Louis Boucher ✠ Kansas City, Kan.; University of Kansas School of Medicine, Kansas City, 1918; formerly on the faculty of his alma mater; member of the American Academy of General Practice; past-president of the Kansas Academy of General Practice, of which he was one of the organizers; for many years police surgeon; formerly city health director; served during World War I; on the staffs of the Providence and St. Margaret's hospitals and the Bethany Hospital, where he died Dec. 8, aged 62, of rupture of the abdominal aorta.

Ham, Coyt ✠ Columbia, S. C.; Medical College of the State of South Carolina, Charleston, 1919; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; served on the faculty of his alma mater; at one time superintendent of the South Carolina State Hospital; neuropsychiatric consultant at Veterans Administration Hospital; on the staff of the South Carolina Baptist Hospital and the Columbia Hospital, where he died Oct. 15, aged 63, of coronary thrombosis and myocardial infarction.

Kobza, Valerian Vincent ✠ Rapid City, S. D.; Creighton University School of Medicine, Omaha, 1943; interned at the Creighton Memorial St. Joseph's Hospital, where he served a residency; served in the U. S. Naval Reserve from July, 1945, to July, 1946; in March, 1951, became partner in the Rapid City Medical Center, where he was appointed to the staff on May 1, 1948; chief of the obstetrics and gynecology service at the Bennett-Clarkson Memorial Hospital and St. John's McNamara Hospital, where he died Dec. 16, aged 41, of coronary occlusion.

Avery, Walter James, Fresno, Calif.; St. Louis University School of Medicine, 1916; member of the American Academy of General Practice; served during World War I; for many years physician at the Fresno County Jail; served as a member of the city board of health; died Jan. 5, aged 68, of heart disease.

Barnes, John McGregor ✠ Cambridge, Md.; University of Michigan Medical School, Ann Arbor, 1924; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society and Radiological Society of North America; fellow of the American College of Radiology; for many years director of radiology at Millard Fillmore Hospital, Buffalo; died Jan. 1, aged 56, of coronary occlusion.

Barnhiser, Von Bergen, Camden, Ohio; University of Cincinnati College of Medicine, 1928; interned at the Lincoln (Neb.) General Hospital; member of the Ohio State Medical Association; served during World War II; on the staffs of the Mercy and Fort Hamilton hospitals in Hamilton; died Dec. 18, aged 54, of myocardial infarction.

Benesi, Oscar, New York City; Medizinische Fakultät der Universität, Vienna, Austria, 1904; at one time on the faculty of his alma mater; became associated with the Department of Hospitals in 1944 and served at the Home for Dependents and Metropolitan Hospital on Welfare Island; executive physician at the Bird S. Coler Memorial Hospital and Home; died Nov. 18, aged 77, of cardiovascular disease.

Benitez, Frank Francis Arnelio ✠ Baton Rouge, La.; Louisiana State University School of Medicine, New Orleans, 1941; interned at the T. E. Schumpert Memorial Sanitarium in Shreveport, where he was a resident; formerly a resident at Methodist Hospital in Houston, Texas, and St. Francis Hospital in Peoria, Ill.; member of the American Trudeau Society; served during World War II; died in the Baton Rouge General Hospital Jan. 3, aged 42, of carcinoma of the liver.

Bero, Edward John, Brooklyn, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1898; died Nov. 16, aged 83, of cerebral thrombosis.

Bird, Gustavus C., Philadelphia; Medico-Chirurgical College of Philadelphia, 1902; an associate member of the American Medical Association; died Nov. 17, aged 79, of arteriosclerotic cardiovascular disease.

Bixby, Oliver Edward, Lynn, Mass.; University of Vermont College of Medicine, Burlington, 1908; member of the Massachusetts Medical Society; died Dec. 4, aged 69, of coronary thrombosis.

Boozer, Albert Isiah ✠ Amory, Miss. (licensed in Mississippi 1906); past-president of the Monroe County Medical Society; died in the Gilmore Sanitarium Jan. 8, aged 82.

Boyd, Kenneth Bray ✠ Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1924; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; served during World War II; on the staffs of the Hospital for Women, Mercy Hospital, Maryland General Hospital, and the University Hospital; died Oct. 23, aged 54, of carcinoma of the pharynx.

Burdick, Gordon Granger, Chicago; Chicago Medical College, 1890; died in St. Francis Hospital, Evanston, Jan. 17, aged 92, of arteriosclerosis and diabetes mellitus.

Burke, Richard David, Philadelphia; Jefferson Medical College of Philadelphia, 1895; an associate member of the American Medical Association; died in the Atlantic City (N. J.) Hospital Dec. 30, aged 85.

Candela, Pompeo Benjamin, Wofford Heights, Calif.; Regia Università degli Studi di Roma. Facoltà di Medicina e Chirurgia, Italy, 1929; served during World War II; fellow of the American Association for the Advancement of Science; member of the American Association of Physical Anthropologists and the American Anthropological Association; on the staff of Kern General Hospital in Bakersfield; died in Veterans Administration Medical Center in Los Angeles Jan. 5, aged 49, of hypertension.

Casello, John Baptist, Cincinnati; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1892; died Nov. 7, aged 86, of hypertensive heart disease.

Colman, Albert C. ✠ Chappell, Neb.; Lincoln Medical College of Cotner University, 1907; at one time mayor; died Dec. 29, aged 72, of acute left ventricular failure.

Cox, Ann Caroline ✠ Sandston, Va.; Tufts College Medical School, Boston, 1906; member of the Massachusetts Medical Society; died Nov. 16, aged 96.

Creel, Donald Wood, Angola, Ind.; University of Chicago School of Medicine, 1933; member of the Indiana State Medical Association; on the staff of the Cameron Hospital, where he died Oct. 25, aged 53, of uremia.

Cruice, John Mulchinock ✠ Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1898; served on the faculty of his alma mater; one of the founders of the Doctors' Hospital; at one time chief of staff at St. Agnes Hospital; for many years associated with St. Joseph's Hospital, where he died Jan. 3, aged 82, of coronary occlusion.

Curley, William Henry ✠ Bridgeport, Conn.; Cornell University Medical College, New York City, 1909; fellow of the American College of Surgeons; past-president of the Fairfield County Medical Society; served as president of the city board of health; on the staff of St. Vincent's Hospital; died in Fairfield Jan. 17, aged 69, of coronary occlusion.

Davidson, Edwin Norvell ✠ Linden, N. J.; University College of Medicine, Richmond, 1910; on the staff of the Rahway (N. J.) Memorial Hospital; died Dec. 26, aged 72, of coronary occlusion.

Davis, Ralph Harold ✠ Penn Yan, N. Y.; George Washington University School of Medicine, Washington, D. C., 1917; served during World Wars I and II; school physician; on the staff of Soldiers and Sailors Memorial Hospital; died in Albany Dec. 27, aged 62, of coronary occlusion.

Deibel, Henry William, Wilkes-Barre, Pa.; Medico-Chirurgical College of Philadelphia, 1902; an associate member of the American Medical Association; died Dec. 28, aged 81, of injuries received when struck by an automobile.

Dodds, Charles Richey ✠ Starkville, Miss.; University of Nashville (Tenn.) Medical Department, 1906; died Jan. 17, aged 79.

Donohue, Daniel Joseph, Oceanport, N. J.; Fordham University School of Medicine, New York City, 1911; died Nov. 14, aged 69, of heart disease.

Drake, Paul McCheyne, Palo Alto, Calif.; University of Kansas School of Medicine, Kansas City, Kan., 1916; served during World War I; at one time practiced in Coquille, Ore., and served as health officer of Coos County; died Dec. 14, aged 64, of heart block.

Dunnick, Milton Carl, New Freedom, Pa.; Baltimore Medical College, 1905; died in the York (Pa.) Hospital Dec. 27, aged 77, of arteriosclerosis.

Focer, Raymond Leslie, Weirton, W. Va.; University of Pittsburgh School of Medicine, 1910; an associate member of the American Medical Association; served during World War I; died in the Veterans Administration Hospital in Pittsburgh Jan. 16, aged 72.

Fractman, Meyer Bernard, Pittsburg, Calif.; Chicago College of Medicine and Surgery, 1914; charter member of the staff of Pittsburg Community Hospital; served during World War I; died in Burbank Dec. 25, aged 73, of arteriosclerotic heart disease.

Graf, Carl Herman ✠ Captain, U. S. Army, retired, Boulder, Colo.; Ohio State University College of Medicine, Columbus, 1916; member of the American Academy of General Practice; entered the regular Army Jan. 15, 1920; retired Jan. 17, 1921; died in St. Anthony Hospital, Denver, Jan. 20, aged 62.

Granet, Adolph, New York City; Universitatea din Bucuresti Facultatea de Medicina, Rumania, 1898; served on the faculty of Columbia University College of Physicians and Surgeons; died in the French Hospital Jan. 12, aged 85, of arteriosclerotic heart disease.

Griffith, R. Sumter ✠ Waynesboro, Va.; College of Physicians and Surgeons, Baltimore, 1886; for many years mayor of Basic City; physician and surgeon for the Norfolk and Western Railway and the Chesapeake and Ohio Railway; in 1954 honored by the local firemen of the Waynesboro Fire Company and was given a plaque as a tribute to his long service; on the honorary staff, Waynesboro Community Hospital, where he died Dec. 14, aged 94, of arteriosclerotic heart disease.

Groesbeck, Harvey Paterson, La Mesa, Calif.; Cornell University Medical College, New York City, 1905; an associate member of the American Medical Association; member of the Medical Society of the State of New York; formerly practiced in Schenectady, N. Y., where he was consulting physician at the Ellis Hospital; died in San Diego Oct. 24, aged 75, of cerebral vascular accident.

Hansen, Harry Beauvoir, Setauket, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1915; served overseas during World War I; died Jan. 15, aged 65, of coronary occlusion.

Harris, Max ✠ Bath, Pa.; Temple University School of Medicine, Philadelphia, 1921; on the staffs of the St. Luke's Hospital in Bethlehem and the Allentown (Pa.) General Hospital; died in Philadelphia Jan. 16, aged 58, of acute myocardial infarction.

Hart, Henry Paxton ✠ Massillon, Ohio; Western Reserve University School of Medicine, Cleveland, 1913; on the staff of the Massillon City Hospital; was shot and killed Jan. 21, aged 71.

Hartshorne, William Ocellus, Spiro, Okla.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1899; served during World War I; formerly associated with the Indian Service and the U. S. Veterans Bureau; died Dec. 19, aged 87, of myocardial insufficiency.

Hays, George Robinson ✠ Richmond, Ind.; Western Reserve University Medical Department, Cleveland, 1902; died Oct. 29, aged 76.

Hoeper, George Edward, Mankato, Minn.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1906; died in St. Joseph's Hospital Nov. 24, aged 88, of arteriosclerotic heart disease.

Hope, Hollis Frank ✠ Atlanta, Ga.; Atlanta College of Physicians and Surgeons, 1913; for many years associated with the county health department; died Nov. 2, aged 64, of coronary thrombosis.

Houck, George Emory, Baltimore; Hahnemann Medical College and Hospital of Philadelphia, 1898; died Dec. 25, aged 79, of heart disease.

Kistler, Henry Bay, Newcomerstown, Ohio; Starling Medical College, Columbus, 1902; past-president of the Tuscarawas County Medical Society; died Dec. 9, aged 76, of cerebral hemorrhage.

McIlwaine, Richard ✠ Knoxville, Tenn.; Jefferson Medical College of Philadelphia, 1919; on the staffs of Fort Sanders Presbyterian, East Tennessee Baptist, and St. Mary's Memorial hospitals; died Oct. 25, aged 61, of a heart attack.

Payne, William Everett ✠ Slaton, Texas; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1911; for many years city health officer and member of the school board; on the staff of the Mercy Hospital; physician and surgeon for the Santa Fe Railway; died Oct. 21, aged 68, of rheumatic heart disease.

Pennell, Walter Johnson ✠ Captain, U. S. Navy, retired, Wakefield, Mass.; Harvard Medical School, Boston, 1917; entered the U. S. Navy in 1917 and retired Jan. 1, 1947; health officer of the Northeastern District of the Massachusetts Department of Public Health; fellow of the American College of Physicians; specialist certified by the American Board of Internal Medicine and the American Board of Preventive Medicine; died Dec. 30, aged 63, of heart disease.

Ragan, Stephen Thomas ✠ Los Angeles; University Medical College of Kansas City, Mo., 1911; member of the American Urological Association; served during World War I; on the staff of Queen of Angels Hospital; died Dec. 9, aged 67, of coronary thrombosis.

Rees, Amos Gager, Fort Washington, Pa.; College of Medicine and Surgery (Physio-Medical) Chicago, 1902; died in the Abington (Pa.) Memorial Hospital Dec. 8, aged 74, of carcinoma of the anus.

Ruud, Helga Mariane ✠ Chicago; Woman's Medical College, Chicago, 1889; formerly on the faculty of her alma mater; for 34 years taught at the nurses' school of the Norwegian-American Hospital, where she was on the staff for many years; died Jan. 29, aged 95.

Weeks, Joshua Herbert ✠ New Bedford, Mass.; Harvard Medical School, Boston, 1924; fellow of the American College of Surgeons; member of the staff of St. Luke's Hospital; formerly physician to the New Bedford Board of Public Welfare; past-president of the New Bedford Lions Club; died in the Grace Hospital, Hutchinson, Kan., Jan. 5, aged 58, of ruptured esophageal varix.

FOREIGN LETTERS

BRAZIL

Megacolon.—At a meeting of the Medical Academy of São Paulo, Drs. Arrigo Raia and Oswaldo Mesa Campos stated that megacolon is a syndrome of chronic intestinal stasis, with hypertrophy and elongation of one or more parts of the large intestine for which at operation or autopsy no intrinsic or extrinsic mechanical cause is found. It may be congenital or acquired. In Brazil, the acquired form is the more prevalent. The patients suffer from chronic constipation and enlargement of the abdomen. The diagnosis is based on characteristic symptoms and signs and on roentgenologic examination, which shows elongation and dilatation of the colon. The segment most frequently involved is the sigmoid. Microscopically, degeneration of the cells of the plexuses of Meissner and Auerbach, of varying intensity in the different segments of the colon, is observed. Nutritional deficiency especially of vitamin B_1 may be a causative factor in some patients. Some physicians believe Trypanosoma cruzi causes megacolon. The disease runs a slow progressive course. The most frequent complication is acute intestinal obstruction by volvulus of the sigmoid or by fecal impaction. Medical treatment with laxatives, cathartics, enemas, and dietetic and hygienic measures gives only temporary relief. Colectomy, sympathectomy, sphincterectomy, or regional rectosigmoidectomy have been proposed. Colectomies in which the dilated loop of the colon are excised fail because of recurrence of the disease. Sympathectomies should not be used as they are based on a wrong concept of the pathogenesis of the condition. Sphincterectomies are followed by a high proportion of recurrences. The best surgical treatment is that in which the segment of the colon in which the plexal lesions are most abundant is excised. This usually involves rectosigmoidectomy, with very low resection of the rectum, down to the insertion of the levator ani muscles, and anastomosis of the rectal stump with the sigmoid or descending colon. The speakers recommend that this be performed in three stages: (1) transverse colostomy, with closure of the distal stump; (2) rectosigmoidectomy, with anastomosis of the colon; and (3) closure of the colostomy.

Two articles on the same subject appeared in the *Arquivos dos Hospitais da Santa Casa de São Paulo.* One of these by Dr. E. Maffei presents a conception that is different from that of Raia and other authors. Dr. Maffei studied megaesophagus, megacolon, and dilatations occurring in other hollow viscera from the pathological standpoint and found that they all possessed anatomic and histological aspects characteristic and wholly different from lesions due to the action of exogenous causes. These organs are not only dilated but also lengthened, and they present kinks and folds; their walls are always thick, rigid, and leathery. Histologically there is hyperplasia of the muscular coats. Sometimes the circular layer and sometimes the longitudinal layer is more excessively developed; other times, the development is more evident in patients in whom both layers are equally overdeveloped. The myenteric nervous plexuses develop abnormally. The muscularis mucosae is conspicuous and frequently made up of circular and longitudinal layers. It sometimes contains nervous plexuses where they are not normally found. Ectopic mucosa is commonly met with in the submucosa. The segments above and below the diseased areas may be practically normal, but in some patients there is hypoplasia of the walls, particularly of the muscular layer. These pathological findings are taken as an indication that we are dealing with an embryonic malformation, confirming Bard's conception of a "local visceral gigantism," which is more frequent in the esophagus and colon but which may occur in the stomach, duodenum, appendix, bladder, and ureters. The anomaly apparently remains silent, as is the case with most congenital malformations, causing only minor functional disturbances until the mechanisms of adaptation and compensation cannot be maintained and the functional activities of the organ are so altered as to interfere with the patient's health. The patient then goes to a physician, thus giving the false impression that this was the moment of the onset. Below the area of the dilatation there is a narrowed segment, which is responsible for the theory that the disease was caused by a spasm of a sphincter. The progression of the contents of the digestive tract is due to contractions controlled by the sympathetic system and relaxation controlled by central nervous system centers in the medulla and spinal cord. Since in megacolon the distal segment remains closed, this may be due to impairment of the opening mechanisms located in the central nervous system. In Dr. Maffei's patients, the radiological examination of the vertebral column showed spina bifida or other malformations of the spinal cord or its roots or both. Spina bifida is not, however, always associated with dilatations. Malformations of the spinal cord and its roots are extremely variable in degree, and therefore the consequences are also varied. In megacolon the anomaly points to an altered innervation of the organ by the central nervous system, which would lead to the absence of the relaxing mechanism of the distal segment, giving the false impression of a sphincter controlled by the sympathetic nervous system.

The items in these letters are contributed by regular correspondents in the various foreign countries.

FINLAND

Rheumatoid Disease of the Foot.—Dr. Kauko Vainio in *Annales chirurgiae et gynaecologiae Fenniae* (supp. 1, vol. 45, 1956) reports a series of 1,000 patients suffering from rheumatoid arthritis. Involvement of the feet was observed in 91.3% of 618 women, in 84.9% of 337 men, and in 68.8% of 45 children. The inflammatory stage is not accompanied by deformities. The longer the duration of the rheumatoid involvement, the more deformities of the feet are seen. Increasing age is of much less importance in this respect. The subastragalar and metatarsal joints were involved, often as the first symptom of rheumatoid arthritis, in 66.9% of the adult patients. This affection was followed by flatfoot in 46.5% of the feet examined. With increasing duration of the disease, the mobile flatfoot showed a tendency to change to the rigid deformity. A varus position of the heel developed in some bedridden patients and in patients walking on the outer border of their feet. In a few children, a cavus deformity of the foot developed during a prolonged confinement to bed. Complete stiffening of the subastragalar joints with cessation of the pain occurred relatively late. The ankle joint was involved much less often (8.8%) than the subastragalar and metatarsal joints. Stiffening in an equinus position was rare in this series. Spread foot was found in 33.2%, hallux valgus in 58.8%, and hallux rigidus in 10.4% of the adults. Hammer finger occurred in 53.2% of the patients. In three patients metatarsalgia with typical rheumatoid changes was found. In the region of the heel, rheumatoid lesions such as bursitis of the tendo calcaneus, tendoperiostitis, and nodules were found in 9% of the patients; and 6.5% of the adults had tenosynovitis of the feet. Histological examinations were made on 59 specimens taken from the base of the great toe in patients with hallux valgus and on 70 specimens from metatarsophalangeal joints. Severe inflammatory changes with fibrinoid degeneration and histiocytic proliferation were detected at the points of attachment of the ligaments. When the ligament loses its strength from degeneration and transformation into a soft granulation tissue, external factors easily cause stretching of these structures. The rapid development of all the deformities found in rheumatoid disease of the foot can be explained in this way. The histological changes found in bursitis of the tendo calcaneus and in the tendon sheaths were similar to those appearing in rheumatoid joints.

Tuberculosis in the Finnish Armed Forces.—Prof. Jorma Pätiälä in *Acta tuberculosea scandinavica* (supp. 35, 1955) reported his study of 2,816 men in whom initial tuberculous pleurisy developed while they were serving in the armed forces in World

War II. The incidence was significantly affected by the activity at the front, the season of the year, and the age and military rank of the patient. In the younger age group the incidence was higher in those from rural districts than in those from towns. So-called late primary infection probably played some part in this difference. The patients were observed for seven to nine years after the onset of pleurisy. In this period postpleuritic tuberculosis occurred in 43.1% of the men, pulmonary tuberculosis alone accounted for 30.2%, and extrapulmonary tuberculosis for 8.8%. The interval between postpleuritic tuberculosis and the initial pleurisy was generally short. The tuberculosis was discovered either at the same time as the pleurisy or within one year of its onset in 40.8% of the patients, within the first three years in 83.4%, and within more than five years in only 5.6%. Familial tendencies to tuberculosis played an important part in the incidence of postpleuritic tuberculosis. The patients who had only pleurisy recovered well. As early as within one year of the onset, 75% of these patients were fully fit for work, and, at the end of the observation period, only a few showed slight disability, due in the main to pleural thickening. The patients with postpleuritic tuberculosis included only 25% who were fully fit for work nine years after the onset of pleurisy, and their case fatality rate was 37.3% (15.6% in the whole series). The percentage of cure was distinctly lower for those who had pleurisy during the first two years of the war.

INDIA

Infiltrating Ependymoma.—Iyer and Monteiro in *Neurology* (**3:** 15 [July-Dec.] 1955) reported a postmortem finding of an ependymal tumor in the left frontal lobe, which extended down into the base of the brain and invaded the dura and bone of the base of the skull. Although glial tumors grow widely in the substance of the brain, they rarely transgress the barrier of the dura to extend into the skull in the absence of any surgical intervention. The subject had been a 52-year-old man who was admitted for unconsciousness of sudden onset and of 12 hours' duration. He had been subject to occasional attacks of giddiness and convulsions. Rales and rhonci were heard on the right side of his chest. His right pupil was contracted and did not react to light. The tone was increased in the muscles of his extremities. This was associated with spasticity, exaggerated tendon reflexes, absence of abdominal reflexes, and a bilateral Babinski's sign. His leukocyte count was 13,200 per cubic millimeter, with 76% neutrophils and 24% lymphocytes. His blood urea nitrogen was 28 mg. per 100 cc. On the day after admission his pupils were equal and fixed, and there was retraction of his neck. His spinal fluid was blood-stained. Hemiplegia developed on the right side. His mental state cleared up, but four days later both pupils were equal and reacted to light. The spinal fluid was still blood-stained, and it revealed normal pressure, 3 cells per cubic millimeter, increased globulin, 187.2 mg. per 100 cc. of sugar, and 800 mg. per 100 cc. of chlorides. The temperature rose, the pulse rate was 150 per minute, and the respiratory rate was 52 per minute. He died with a terminal rise of temperature. An autopsy showed scattered areas of bronchopneumonia. The cerebral hemispheres were congested and appeared to bulge out. The orbital surface of the left frontal lobe was adherent to the orbital plate below. On separating the adhesions a hemorrhagic mass measuring 3 by 4 cm. was seen arising from the left frontal lobe. The dura over the orbital plate was markedly adherent, and the underlying bone was eroded by the mass. The cerebral hemispheres showed changes indicative of increased intracranial pressure. There was an oval ragged mass at the base of the brain, occupying the region of the orbital gyri and encroaching behind on the olfactory tract. Both the lateral ventricles were dilated and contained blood-stained fluid. A round mass projected into the cavity of the anterior horn of the left lateral ventricle, which was completely covered with ependyma. It extended into the left frontal lobe. The center of the mass was necrotic and showed evidence of a recent hemorrhage. The white matter around the mass was rarified. The histological features were characteristic of ependymoma with uniform cellularity and rosette formation. There were a number of mitotic figures.

Abdominal Pregnancy.—Sur Roy and Chaudhari (*J. Indian M. A.* **25:**525 [Dec. 1] 1955) reported a case of intraligamentary secondary abdominal pregnancy that was diagnosed clinically. A laparotomy was performed and the gestation sac was removed with sacrifice of only the affected oviduct. The patient, a 30-year-old nullipara, was admitted to the hospital with an abdominal mass of two years' duration, associated with slight pain at times. She gave a history of amenorrhea occurring two years previously and lasting for two months, which was followed by abdominal pain and profuse vaginal bleeding. The pain subsided, but irregular vaginal bleeding continued for 10 months and was associated with progressive enlargement of the abdomen. Menstrual periods for the next year were regular but discharge scanty. The swelling receded a little, but there were a few attacks of mild abdominal pain. The swelling was situated in the hypogastric region and extended to the umbilicus; it was hard, with well-defined margins, and was slightly mobile from side to side. No fetal parts could be palpated. On vaginal examination the cervix was firm, small, and nulliparous. The lower pole of the swelling could be felt behind the cervix, and the fetal head, with yielding cranial bones, could be palpated in the mass. The uterus was displaced forward and normal in size. A roentgenogram of the abdomen showed the fetal skeleton with overlapping of the cranial bones. A hysterosalpingogram showed the dye in the uterine cavity without any spilling into the peritoneal cavity. On opening the abdomen the gestation sac was found to be 8 in. in diameter and situated between the left lateral pelvic wall and the uterus. The left tube was stretched over it and the left ovary was also adherent. The sac extended between the two walls of the pelvic mesocolon. There were hardly any adhesions. The sac contained a mummified fetus and a shrunken placenta. The placenta had no additional attachment with the omentum or intestines. The right tube was thickened and closed at the fimbriated end. The right ovary was normal. The sac and left oviduct were removed, leaving the left ovary. Salpingostomy was performed on the right blocked tube. Recovery was uneventful.

Treatment of Salmonellosis.—Banerje and Maiti (*J. A. Phys. India* **3:**135 [Oct.] 1955) studied a series of 307 patients with typhoid who were admitted to the Medical College Hospital, Calcutta, during the periods, 1948 through 1949 and 1953 through 1954. The latter group was treated with chloramphenicol. Of these, 284 were infected with Salmonella typhosa, 17 with S. paratyphi, one with S. schottmülleri, 2 with S. hirschfeldii, and 3 with mixed types. Blood cultures showed that the younger the patient the greater the incidence of positive blood cultures. The formation of the antibodies that produce the Widal reaction is not interfered with by the antibiotic treatment. Chloramphenicol reduced the death rate from 18.5 to 6.4%, but the rate in the first decade of life was not appreciably affected. It also reduced the incidence of complications except for hemorrhage, which was slightly increased. Fever decreased within five days in 49.2% of the patients treated with chloramphenicol, and their relapse rate was also reduced. When relapse occurred, the response to chloramphenicol was prompt. In this series, 6.1% of the patients showed no appreciable response to the antibiotic.

Blood Histamine in Patients with Eosinophilia.—Achari and Acharya in the *Patna Journal of Medicine* (**29:**595 [Dec.] 1955) reported their study of the histamine content of normal human blood and that of patients showing different grades of eosinophilia. Adult male and female subjects were selected at random. An absolute count of eosinophils was made. A total count of 250 to 750 per cubic millimeter was considered to be within normal limits. The blood histamine values for these persons ranged from 0.015 to 0.031 mcg. per cubic centimeter, while in patients with eosinophilia they ranged from 0.025 to 0.052 mcg. per cubic centimeter. Thus there was a significant increase in the histamine content of the blood in eosinophilia. No relation, however, could be established between the degree of eosinophilia and the blood histamine concentration.

Falciparum Malaria.—M. P. Misra (*J. A. Phys. India* **3:**144 [Oct.] 1955) has presented an analysis of 60 cases of malaria, caused by Plasmodium falciparum, with pernicious manifestations. The case fatality rate was higher in children than in adults. The

incidence of the disease was higher between July and October. The diagnosis was based on the presence of the plasmodia in the peripheral blood, a history of intermittent fever, and a palpable spleen. The leukocyte count may be normal or raised with an increase in the neutrophils. A leukocyte count of 20,000 per cubic millimeter or more does not exclude the possibility of falciparum malaria. It was noticed that malarial parasites were scanty in the peripheral blood in patients with falciparum malaria, with pernicious manifestations at the height of the fever. Although gastrointestinal manifestations were commonest in falciparum malaria, the patients admitted to the hospital usually had the cerebral type. The algid type was comparatively rare. Fever may be intermittent, irregular, or remittent, the last being the commonest. Pernicious manifestations may supervene any time during the course of the disease, but only rarely did they appear suddenly at the start of the illness. An increase in monocytes was not observed during an acute attack. The usual treatment was an intravenous injection of quinine, but the mortality was high and this procedure had the following drawbacks: 1. It lowered the blood pressure, thus causing deterioration of the general condition unless the injection was given by the drip method. 2. The drug disappeared quickly from the blood. 3. In patients with an idiosyncrasy to quinine it led to death. 4. It was found to be capable of precipitating blackwater fever. Intramuscular injections of quinacrine and intravenous injections of chloroquine gave the best results in patients with acute falciparum malaria with pernicious manifestations.

Hepatic Cirrhosis.—Sarin and Mital in the *Antiseptic* (**52:**837 [Nov.] 1955) state that liver extract given intravenously has a definite place in the treatment of cirrhosis of the liver and hepatitis. They used crude liver extract in the hope that the proteins present would have a better protective action than other proteins. Crude liver extract from 10 gm. of raw liver, with 25 mcg. of vitamin B_{12} and 5 mg. of folic acid, 100 mg. of nicotinamide, and 25 mg. of choline dihydrogen phosphate per cubic centimeter, was diluted and given with dextrose intravenously to patients with cirrhosis of the liver. Twenty patients were given 475 injections in all. No other drug was used and no extra protein was added to the diet. An initial intradermal test for sensitivity was made and, if no reaction was obtained, 0.5 cc. of the product diluted with 10 cc. of 25% dextrose was given slowly by vein on the next day. The dose was increased by 1 cc. every day to a maximum of 5 cc. The first 15 injections were given daily and later doses on alternate days. No ill-effects developed after the injections except for a mild urticaria in one patient and slight flushing of the face in two patients at the beginning of the treatment. Clinical improvement was recorded in 16 of the 20 patients, as judged by a feeling of well-being, increased appetite, and disappearance of ascites in 6. Liver biopsy performed on some patients showed evidences of improvement.

Retained Placenta.—In the *Journal of Obstetrics and Gynaecology* (**16:**187 [Sept.] 1955), O. Francis reported on a series of 313 women with retained placenta. The maximum incidence was met with in primiparas in the age group 21 to 30 years. In 30.4% the birth was premature. The placenta was adherent in 67.4%, and in 79% it was removed manually. In 16.6% of the latter group manual removal was done for simple retention of a placenta that could not be expressed, and, in the rest of this group, the placenta was adherent. Postpartum hemorrhage occurred in only 48% of the women with adherent placenta. Manual removal when done promptly and proficiently was found to be a safe procedure, sepsis developing in only 4.8% of the cases. Ergonovine helped to control the hemorrhage associated with retained placenta, but its action in expelling the retained placenta was found to be unreliable. Of the patients who had been delivered at home, 9.5% were brought in in a moribund state and died within a few hours and 25% (29 patients) were in a state of collapse; 2 of the latter died. Retained placenta accounted for 7.4% of the maternal deaths in the hospital. The chief causes of death were shock, hemorrhage, and sepsis.

ITALY

Nutrition Conference.—The third Nutrition Conference was held in Rome in September. Dr. Harris of England said that the function of the adrenal cortex is essential for the preservation of life. Its action is particularly important in sexual development and in electrolyte, water, carbohydrate, and protein metabolism. The adrenal medulla secretes epinephrine and also arterenol. Corticotropin, secreted by the anterior lobe of the pituitary, causes an increase in the secretion of the adrenocortical hormones. Among the nutritive factors that are of interest with regard to the adrenals are the vitamins. Dr. Harris does not believe that a specific correlation has been found between pantothenic acid and the activity of the cortical hormones. Although at first there seemed to be some evidence of a close link between the action of vitamin C and the adrenal function, the speaker believes that the hypothesis of the action of vitamin C being concentrated in the adrenal gland has not been proved.

Dr. Marañon of Spain said that theoretically patients with Addison's disease should be given a diet rich in carbohydrates, fats, and lipids, with a sufficient amount of proteins, foods rich in sodium chloride and poor in potassium, and large amounts of vitamins C and B. On the other hand, patients with hypercorticalism should have a moderate-carbohydrate, high-protein, low-fat diet with some reduction in chlorides. However, on the basis of clinical experience, the speaker believes that it is often useless and sometimes even dangerous to apply such theoretical knowledge too rigorously to human nutrition, especially in the case of an ill person. In view of modern chemotherapy, the diet of patients with adrenal diseases is of secondary importance. The one rule that must not be forgotten is that the diet should contain the necessary quantity of sodium chloride.

Professor De Mole and Dr. Fabre of Switzerland stated that patients to whom cortisone is being given should receive a chloride-poor diet and a supplement of potassium, nitrogen, and calcium if the heart is diseased. A diet restricted in carbohydrates and glucosides is necessary in the presence of a disturbance of the carbohydrate metabolism. In patients treated with cortisone and corticotropin who do not show adrenal insufficiency, the aim should be to check the sodium retention and the potassium loss. In chronic diseases, in addition to the sodium-calcium equilibrium, the loss of nitrogen and the tendency to hyperglycemia have to be checked.

Professor Peretti of Italy said that in a well-balanced diet the total caloric content, the balance between the various energy and tissue-building components, the mineral and vitamin balances, and the relationship with special physiological conditions, such as those arising out of the period of growth, pregnancy or nursing, and heavy work, must be considered. The recommended daily amount of protein for the average man is about 1 gm. per kilogram of body weight, with proteins providing 8 to 11% of the total caloric content of the diet. The average daily intake of carbohydrates should provide 60 to 70% of the total caloric content of the diet. There is no fixed quantity for lipids, because they can be used interchangeably with carbohydrates, but 20 to 25% of the total caloric content of the diet should be made up of fats. The daily requirement for calcium is about 0.8 gm.; for iron, 12 to 15 mg.; and for phosphorus, 1 to 1.5 gm. It is difficult to establish definite vitamin requirements because there is a certain amount of overlap in their functions.

Professor Randoin and Dr. Causeret of France said that increases in some nutritious constituents of a food can be obtained either by direct introduction or by applying some physical treatment, such as irradiation with ultraviolet rays. They distinguished natural from artificial enrichment and concluded that, when it is necessary to enrich a food, it is always preferable to do so by a natural process. Artificial enrichment should be permitted only under special circumstances and should not be done routinely.

Congress of Urology.—At the 28th congress of the Italian Society of Urology in Trieste in September, Professor Pisani of Milan said that, using a modification of the pararectal approach, perineal prostatectomy is well tolerated and can be performed on patients who are greatly emaciated or obese; in fact, for such patients perineal prostatectomy is preferable to other techniques. The danger of urinary incontinence and impotence is negligible,

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and the operation can be performed quickly and is not traumatizing. Professor Gallizia of Turin reported good results with his modification of the retropubic technique for prostatectomy. Prof. Mario Fernandez of Palermo said that, despite the fact that there are more modern techniques than transvesical prostatectomy, Freyer's operation still gives satisfactory results and should be considered in selected cases. Its chief disadvantage is that the patient must be hospitalized longer than with other techniques. Professor Cominelli of Naples said that Hryntschack's one-stage prostatectomy, using the transvesical approach and obtaining hemostasis by suturing the prostatic bed and the vesical neck, is well tolerated, brings about perfect recoveries, and permits a better hemostasis than the other methods. For these reasons the School of Naples, which had at first supported and encouraged Millin's retropubic operation, today prefers this operation, while recognizing the value of the other methods.

Professor Nicolich of Genoa said that endoscopic electroresection does not remove all the adenoma and therefore, strictly speaking, is not a prostatectomy. This method has not been widely accepted in Italy. All the techniques discussed can be used to correct the process with a minimal risk of death and with satisfactory immediate and late results. A careful preliminary study of the patient, especially examination of his renal function, evaluation of the indications, and good postoperative care help to reduce to a minimum the dangers of the operation. Some surgeons operate routinely only when the disease is in the second or third stage and operate on those whose disease is in the first stage only if the patient has grave subjective disturbances. Others operate routinely when the disease is in the first stage. Whatever operative procedure is used, constant control of the arterial pressure during the operation is essential, because a drop in pressure could result in some vessel's escaping hemostasis and thus lead to postoperative hemorrhage. This implies that prostatectomy should never be performed in patients in whom hypotension is induced by ganglioplegics.

Endemic Primary Encephalitis.—At the meeting of the Italian Society of Internal Medicine in Rome in October, Professor Condorelli of Rome stated that, after the great epidemic of epidemic encephalitis, numerous endemic foci or restricted epidemics of acute diseases of the nervous system were reported in many countries of Europe. They were clinically primary, of a definitely infectious nature, and almost always associated with a secondary meningeal inflammatory reaction. In 1939 Professor Condorelli observed in eastern Sicily a large number of acute nervous infections that were followed by a high percentage of recoveries without any sequelae. The constant negative results of all the standard bacteriological and serologic tests confirmed the etiological independence of this encephalitis from the encephalitides caused by known viruses. It was therefore called Sicilian-Calabrian encephalitis. It usually manifests itself in sporadic cases and only exceptionally in the form of small epidemics. It is commoner in men than in women and does not exhibit a seasonal peak. On the basis of the course and the parts of the cerebrospinal axis that are involved, the following forms can be distinguished: acute meningoencephalitis, subacute meningoencephalitis, and forms that are mainly peripheral. Generally, the symptoms of acute encephalitis regress with surprising rapidity, and complete recovery may occur in three or four weeks. The course of subacute meningoencephalitis may vary from two months to three years. The peripheral forms are of the polyradiculoneuritic type, with constant involvement of the brain and spinal cord. Bulbar paralysis is a rare complication of this form. Because the pathogenic agent is still unknown, there is no specific therapy. In some patients good results have been obtained with antibiotics, especially chlortetracycline and chloramphenicol.

PERU

Parietal Tumors Without Parietal Signs.—Tumors of the parietal lobe do not always cause the so-called parietal signs. Absence of these signs does not, therefore, rule out a parietal tumor according to Prof. A. Asenjo and his co-workers in the *Revista médica del Hospital obrero* (vol. 4, no. 3, 1955). The authors studied 104 patients with neoplasms, malformations, and granulomas involving the parietal lobe and found that 56 of them showed no parietal signs. The "exclusive parietal syndrome" consists of astereognosis, vegetative and trophic changes, and pseudothalamic signs and disorders in thermalgesia, discriminative and deep sensibilities, coordination, reading, and calculation. The patients were divided into a conscious group and a confused, or stuporous, group. In both groups the percentage of patients with no parietal signs was similar. Of the 72 conscious patients, 37 did not show parietal signs at any time, and, of these, 11 had lesions affecting only the parietal lobe. One patient had an infiltrating astrocytoma that was neurologically silent, and the other 10 had extracerebral lesions, mostly hemangiosarcomas that compressed the parietal cortex but did not pierce it. This caused motor deficit phenomena in 8 of the 10, while 2 were neurologically asymptomatic. The remaining 26 of the 37 conscious patients had lesions that involved the parietal lobe and other cerebral lobes, but only 20 of them showed any neurological signs. Of the 32 patients in the second group, 19 had no parietal signs. Of these, 3 who had lesions involving the parietal lobe alone showed no neurological signs other than changes in consciousness, and the remaining 16 had lesions involving several lobes. Two of the latter were free from detectable neurological signs. In both conscious and confused patients with neurologically symptomatic lesions involving more than one lobe, the most frequently detected signs were motor deficit phenomena, disturbances in the visual field, aphasia, apraxia, and cerebellar symptoms. The paretic states were by far more frequently found than the paralytic ones. The authors called attention to the fact that, in general, right-handed patients with extensive intracranial lesions on the left side did not show aphasic or apractic signs, displaying only paresis or paralysis.

Postoperative Carbohydrate Metabolism.—After abdominal operations the satisfaction of the caloric requirements of the patient and the maintenance of an adequate fluid-electrolyte balance are the surgeon's most important problems. Drs. Luis Carrillo Maúrtua and Abelardo Ulloa of the Dos de Mayo Hospital of Lima studied the carbohydrate balance of patients in whom potentialized anesthesia by means of hibernation was used. They reported their results to the second National Congress of Medicine in Lima in October. Twenty patients were studied. Prior to operation, Exton and Rose's glucose tolerance test was performed in all. During the immediate postoperative period, 10 patients were given 2 liters of 5% dextrose solution daily and 10 received 2 liters of 10% dextrose solution daily. In both groups the blood sugar level rose to the upper limit of normal, but in no case was an abnormal level reached. The average percentage of the increase was 9.4. Glycosuria in the first group became evident after the second postoperative day, and it represented a daily glucose loss of 5 to 9% of the total given. In the second group glycosuria became evident on the first postoperative day, and it represented a daily glucose loss of 8 to 14% of the total given. The diuresis was not significantly influenced by the concentration of the dextrose solution, which was always given intravenously. The speakers concluded that, by using the 10% dextrose solution, the surgeon nearly meets the minimal caloric requirements that every patient undergoing an abdominal operation needs in the postoperative period. This applies also to every patient who, after the third postoperative day, is still unable to take food by mouth. Although the quantity of dextrose given daily can be increased, the speakers recommend that the total volume of fluids not exceed 2.5 liters.

Spinal Anesthesia.—Dr. Pedro Carlín in *Revista médica del Hospital obrero* (vol. 4, no. 3, 1955) states that various neurological complications may arise early or late in the postoperative period following spinal anesthesia and that they may show variable intensity and duration. They appear to be unrelated to the type of anesthetic used. Dr. Carlín reviewed the clinical records of 1,100 surgical patients in whom spinal anesthesia was used and found that 125 (11.36%) had postoperative neurological complications. Headache was by far the most frequent disturbance, as 112 patients complained of it. The cauda equina syndrome was observed in eight, transient abducens paralysis in two, and septic meningitis, aseptic meningitis, and meningismus each in one. The less the damage produced by the spinal tap, the less the likelihood of such complications. If a patient who is to be operated on shows any abnormal neurological sign, the use of spinal anesthesia is contraindicated.

SPAIN

Literary Awards.—The Association of Medical Writers and Artists awarded their gold medal to Dr. Carlos Blanco Soler, their president, for the help and protection he has given the association. Among others, Dr. Leon Goldman of Cincinnati was given honorable mention and a bronze medal, one of the Blanco Soler awards for 1955. The same awards for 1956 are open to physicians all over the world. They are given for work on art, history, literature, and philosophy in relation to medicine. There will be a first prize of 5,000 pesetas and a gold medal, a second prize of 2,500 pesetas and a silver medal, and a number of honorable mentions with bronze medals. The articles may be written in any language, should be typed in duplicate distinguished by a code name (the real name to be enclosed in a sealed envelope), and sent by registered mail to Dr. J. Fernán Pérez, Secretario General, Fuencarral, 113, Madrid, Spain.

Public Health.—The General Director of Public Health reported a crude death rate of 9.2 per 1,000 and an infant death rate of 48 per 1,000. In 1954 there were no cases of smallpox or louse-borne typhus. There were 2,000 cases of malaria reported, as compared with 500,000 in 1941. The total number of cases of poliomyelitis reported was 1,000. Poliomyelitis vaccine will be given to children as soon as its value and safety have been established. The total number of deaths from tuberculosis was 11,000; the incidence of this disease was greatest in the southern regions and greater for men than for women. The incidence of leprosy has decreased to such a degree that the leprosarium under construction in Toen, Galicia, will be used instead for psychiatric patients.

SWEDEN

The Dissatisfied Patient.—The medical press has recently contained an exchange of opinions with regard to the complaints against physicians, nurses, dentists, and pharmacists brought to the notice of the Swedish Physicians' Liability Committee. Every year about 200 such complaints are dealt with, and about 80% of them are dismissed as unwarrantable. In view of the fact that the number of patients treated each year runs into seven figures, the numerical significance of these complaints may seem small, but the handling of them by the committee has caused resentment in some quarters. One critic would like the committee not only to dismiss complaints as unwarrantable but also to censure the complainants, so as to discourage them from similar action in the future. Fortunately the respectable lay press refuses to publicize this class of complainant. The nuisance value of the sensational lay press in this matter is, however, great. A typical complaint concerns the patient who is refused admission to a hospital and is subsequently found to have been in serious need of hospitalization. Wise after the event, all concerned may deplore the mistake made in such a case, but, as a hospital surgeon points out, if a doctor were to admit the patient in every doubtful case on the chance of a serious injury or illness, he would for long spells have to refuse admission to every patient with a chronic illness. He doubts that the fear of complaints would in itself make his colleagues more efficient in the field of diagnosis and treatment, but he foresees that this fear may encourage a tendency to shift responsibility, to pass the patient on to colleagues, or to let him run the gauntlet of many unnecessary tests.

Hay Fever.—Dr. H. Arnoldsson in *Nordisk medicin* for Dec. 22, 1955, reports that, of 503 patients undergoing specific hyposensitization before the start of the pollen season, 400 were observed for several years. The perennial treatment given to these patients was repeated for two or three years, the first series of two or three injections weekly being followed by a maintenance injection every fourth week. Improvement was noted in 75% of these patients and complete freedom from symptoms in 34%. In Arnoldsson's opinion, antihistaminic treatment has proved a strong competitor of specific hyposensitization. Of 82 patients given antihistaminic treatment, 60 obtained lasting benefit, but the symptoms of the others recurred when this treatment was discontinued. Twelve patients whose hay fever was refractory to both specific hyposensitization and to antihistaminic treatment were given 25 mg. of cortisone three times daily, the dosage being gradually reduced to 25 mg. once a day throughout the pollen season. With these small doses no side-effects were observed, and improvement or cure was observed in all but two patients. Since the action of antihistaminics and cortisone is only symptomatic and will not result in a permanent cure, Arnoldsson believes that specific hyposensitization is still the treatment of choice.

Treatment of Gonorrhea.—Dr. Anders Lodin in *Svenska läkartidningen* for Jan. 5, 1956, reports that an initial injection of one million units of procaine penicillin, as formerly used in treating gonorrhea, is unnecessarily high. After such a dose in a group of patients, a few complications were observed and the recovery rate was less than 100%. Since July 1, 1954, he has reduced the dose to 300,000 units; in 165 patients thus treated, he has not seen a single complication, and he can claim a recovery rate of 100% if due account is taken of reinfections during treatment. No penicillin-resistant strains of gonococci have been seen, and the author is inclined to doubt their existence.

UNITED KINGDOM

College of General Practitioners.—The third annual report of the College of General Practitioners, which is published as a supplement to the December issue of the *Practitioner*, shows that the membership has increased by 320 to 3,287. Of the total, 465 reside overseas. New overseas faculties are being developed in Cork (Ireland), in Perth (Western Australia), and in Christchurch and Dunedin (New Zealand). Members and associates of many faculties are taking students into their practices. In two faculties about one-third of the members are doing so, and in one of the Scottish faculties nearly all members of the faculty have had students attached to them for a period of two to four weeks. Lectures by general practitioners to medical students are taking place in many faculties. One Yorkshire faculty has arranged an annual meeting between final-year students and general practitioners, and ward teaching by general practitioners is being arranged in Edinburgh, Scotland.

There are few medical schools now in which general practitioners do not give some of the instruction. Several medical schools have instituted courses by general practitioners, and more are sending their students to visit general practices. The college is compiling a list of general practitioners throughout the country who are willing to take students. Such a register should enable any student to be placed with a general practitioner suitably near his home or his medical school. In a report to the General Medical Council on the revision of the medical curriculum the college has stressed the importance of remedying the present overcrowding of the curriculum and recommends drastic pruning. The college has also recommended that medical students should continue to be taught the technique of minor surgery, because in the future more minor-surgical operating rooms will be open to general practitioners, and that, given the right conditions, minor surgery should always come within the purview of the family physician. The college also believes that in view of the certainty that nearly every general practitioner will at some time be confronted with a face presentation, problems of abnormal obstetrics should not be relegated entirely to postgraduate specialized training. Another recommendation is the development, as soon as possible, of a department of general practice in each medical school. Such a department would be responsible to the dean of the medical school and would coordinate the teaching of those subjects that pertain to general practice. It would be directed by a physician in active general practice. Although the department would be mainly concerned with undergraduate education, it could not effectively discharge its function or achieve true academic status without making an active contribution to postgraduate training and to research in the field of general practice.

The research activities of the college include an investigation into the efficacy of sulfonamides and antibiotics in preventing the complications of measles. In collaboration with the Registrar General's department a national morbidity survey is being carried out. It includes contributions from over 100 practices

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in which every service performed by the practitioner is being recorded. A register of practitioners interested in the conduct of clinical trials of new drugs has been prepared, but the college does not intend to sponsor therapeutic trials of substances in which a vested financial interest exists. On the other hand, it is believed that the actions of drugs in common use would repay closer study.

At its annual meeting in 1954, an ad hoc committee was appointed to consider an examination as a possible method of selecting its membership. The committee concluded that such an examination is practicable and that it should consist of written, clinical, and oral parts. The committee has prepared a provisional syllabus for such an examination. This contains a list of over 500 clinical, technical, medicolegal, and administrative subjects with which a general practitioner commonly has to deal.

Unethical Conduct Charged.—At its recent session the medical disciplinary committee of the General Medical Council had before it the case of Dr. John Kelvin, of Glasgow, Scotland, who appeared on a charge of unethical conduct. In an effort to promote his professional career, he had associated with an organization known as the Akers' Hair and Scalp Clinics in the United States, which had systematically procured or sanctioned the publication of reports and advertisements directing attention to his professional skill, knowledge, services, and qualifications in various newspapers in the United States. Further, it was alleged that he held a press conference in Chicago in October, 1954.

The solicitor for the council stated that, in a letter published in the *British Medical Journal* in September, 1954, Dr. Kelvin reported that two patients, for whom he had prescribed β-pyridylcarbinol tartrate for intermittent claudication, volunteered the information that the tablets had grown a good crop of hair on their bald heads. This perfectly correct procedure involved him in a blaze of world-wide publicity, as a result of his letter's being taken up by the popular press. Among his many visitors was the director of the Akers Hair and Scalp Clinics, who offered to open a research laboratory in Glasgow, with Dr. Kelvin as research director at a salary of $10,000 a year. Provisional terms were agreed upon, and in October Dr. Kelvin flew to the United States to sign the contract, having written to the General Medical Council asking that his name be removed from the Medical Register. There was a press conference in Chicago, at which Dr. Kelvin was photographed examining a bald head, but no contract, and Dr. Kelvin returned to Glasgow. Negotiations continued, and meanwhile the Akers Clinics inserted numerous advertisements in American papers. One advertisement contained a letter alleged to have been written and signed by Dr. Kelvin. Dr. Kelvin denied authorship of this letter, and the council's solicitor stated that the signature did not appear to be his. Dr. Kelvin went again to the United States, and when he returned to Glasgow in 1955 the research clinic had become a mirage. Meanwhile he had been informed by the General Medical Council that certain formalities had to be complied with before his name could be removed from the Medical Register.

In the witness box Dr. Kelvin said that when he went to the United States he was shocked to find that he was dealing with crooks and profiteers and that he had lost more than he had gained from his association with Mr. Akers. He was to have been reimbursed for all his expenses on his trip to the United States, but when he got there the Akers organization refused to pay his hotel bill. When he returned to Glasgow he received four sporadic payments of $500. The committee found the facts set out in the charge to have been proved, but, although they viewed the case with grave concern and considered the evidence sufficient to support a charge of unethical conduct, they postponed judgment for two years. Dr. Kelvin will be required to appear before the committee in November, 1956, and again in November, 1957, with evidence of his conduct in the interval.

Aspirin and Gastric Hemorrhage.—Further evidence that aspirin can cause gastric hemorrhage in susceptible persons has been presented by Dr. A. P. Waterson, who studied a series of 151 patients admitted to the hospital with hematemesis and melena (*Brit. M. J.* **2**:1531, 1955). Thirty-four of these patients never took aspirin, and of the remaining 117 a proved or probable peptic ulcer was diagnosed in 106. Twenty-eight patients complained of dyspepsia, nausea, heartburn, or vomiting after taking aspirin. There was no correlation between the method of taking the aspirin and the occurrence of symptoms. Some patients swallowed whole tablets, with or without water, and others crushed them first. Apparently some patients with peptic ulcer treat their pain not only with alkalis but sometimes with large doses of aspirin; 17 in this series admitted to taking aspirin for the relief of abdominal pain, 5 of them regularly. In three patients there was reasonably good evidence that aspirin could be incriminated as the cause of hemorrhage in the absence of any other gastric lesion. In the hospital, patients rarely refuse medicines, and those who normally avoid aspirin and its preparations because of its side-effects may not think this worth mentioning when offered tablets during hospitalization. Some hematemesis occurring in the hospital, which is unexplainable, may in fact have been provoked by aspirin. Waterson recommends that patients should always be questioned about their aspirin habits in any case of gastrointestinal bleeding, particularly as those in severe pain may take far more than the normally prescribed dose. He advises that patients with gastrointestinal symptoms should take aspirin as calcium or neutralized aspirin, or in the form of enteric-coated tablets.

Shortage of Dentists.—The main provisions of the proposed dentists' bill are: (1) the formation of a general dental council, (2) simpler procedure for admitting foreign dentists, (3) restrictions on the practice of dentistry, and (4) recognition of dental hygienists. The most important feature was the grant of self-government to the profession. The council was to have 35 members, including 31 registered dentists. The admission of foreign dentists applied to about 55 persons. If their diplomas could not be checked, the council could register them after an examination. The ratio of dentists to the population is 1:3,400, or about one-third of the number needed for efficient service. The Minister of Health thought that oral hygienists should be able, under the supervision of a registered dentist, to fill or extract the deciduous teeth of school children, but the British Dental Association is opposed to the introduction of ancillaries and did not think that the experiment would work. It feared that this would lead to a general lowering of standards. Miss Hornsby-Smith, of the Ministry of Health, pointed out the increasing demand for dental care at a time of grave shortage of dentists. Children entering school at the age of 5 had, on the average, five teeth missing, decayed, or filled. About 67% of all children up to the age of 14 do not go to a dentist in any given year. It is a reflection on parents that they willingly take their children to a hairdresser but do not willingly take them to a dentist.

Interclass Marriages.—There is much interchange between social classes at marriage, so that, for example, many daughters of skilled manual workers marry men in the professional and managerial classes or men in semiskilled and unskilled occupations. Women who married into a higher social class were usually taller and in better health, were better educated, and came from smaller families than those who remained in the same class or who married into a lower social class. The effect of this process on the rates of prematurity and obstetric death of the social classes in Aberdeen has been examined by Illsley (*Brit. M. J.* **2**: 1520, 1955). Records were obtained of 3,911 married primiparas. Intelligence test data were also obtained in a special study of a sample of 278 hospital primigravidas. Those women who rose in social status at marriage already possessed advantages in terms of growth, health, and education, and, as might be expected, they had lower prematurity and obstetric death rates than those who moved into a lower social class at marriage. Although the tendency today in civilized countries is for a general social leveling, the process of social selection by women at marriage may continuously obscure the effects of this leveling by keeping open the gap in the social classes. The inevitable delay in translating social improvements into improved health and the greater rapidity with which the upper social classes take advantage of new welfare services and advances in medical knowledge also tend to keep open the gap between classes.

Chemical Test for Carcinoid.—The presence in carcinoids of large amounts of serotonin (5-hydroxytryptamine), and its excretion as 5-hydroxy-indole-acetic acid, has been used as a screening test for the rapid examination of suspected cases of carcinoid by Hanson and Serin (*Lancet* **2**:1359, 1955). A rapid chromatographic test for 5-hydroxy-indole-acetic acid and serotonin that can be done in about an hour has also been devised by Curzon (*Lancet* **2**:1361, 1955). Hanson and Serin found abnormally high amounts—up to 230 mg. (normal 3 to 8 mg.) in 24 hours—of 5-hydroxy-indole-acetic acid in the urine of patients with malignant carcinoid. A single low value is of no significance, and repeated determinations must be made before carcinoid can be excluded. After surgical removal of an abdominal carcinoid, the excretion of 5-hydroxy-indole-acetic acid falls. A study of the excretion of this compound is considered to be of great diagnostic value. A serum serotonin level at least 10 times the normal figure has been reported by Duncan and his colleagues of Carlisle (*Brit. M. J.* **2**:1586, 1955) in a case of argentaffinoma (carcinoid) of the ileum with hepatic metastases.

Reciprocal Agreement or Social Security.—A reciprocal agreement on social security between the United Kingdom and New Zealand will come into operation on April 1, 1956. Under the agreement the Ministry of Pensions and National Insurance in the United Kingdom will treat persons who come from New Zealand as if they had paid contributions to the national insurance scheme while they were in New Zealand, so as to enable them to qualify for retirement pensions, widows' benefits, and medical, sickness, and unemployment benefits. Similarly persons from the United Kingdom going to New Zealand will continue to receive, as they would in Great Britain, all the benefits that they are entitled to receive under the national insurance and health services. The New Zealand Ministry of Social Security will treat them as if they had been resident in New Zealand while they were living in the United Kingdom to enable them to satisfy the conditions for New Zealand benefits. The agreement also provides for the payment of sickness and unemployment benefits under the New Zealand schemes to people from the United Kingdom.

Minimal Tuberculous Lesions of the Lung.—At a clinical forum held at the Ciba Foundation in London in December, Air Commodore Rumball, discussing the reactivation of a latent tuberculous focus in Royal Air Force flying personnel by the stretching of lung parenchma during rapid or explosive decompression or radial acceleration, said that between 40 and 50% of nodular lesions removed after a course of chemotherapy contained living tubercle bacilli. Such nodules constitute a hazard to flying personnel. The only rational treatment of this type of tuberculosis in fliers is resection. Prof. J. W. Crofton explained that the relapse rate was lower if chemotherapy was prolonged. Dr. J. R. Belcher recommended chemotherapy for six to nine months before operation, which is performed if a relapse occurs after prolonged chemotherapy and if the sputum is persistently positive, if large tuberculomas are present, or if the diagnosis is in doubt. Operation should also be considered for patients unable or unwilling to spend a long time in the hospital and for those uncooperative in taking medication.

A High-Speed Bail-Out.—Flying Officer Hedley Molland made flying history when he survived after bailing out of a plane traveling at supersonic speed. His jet-propelled plane crashed from an altitude of 25,000 ft. into the sea. The Mach meter registered a speed of just under 700 mph, and the plane would not respond to the controls. There was no time to send an emergency radio message to the base. The flying officer, the second man ever to make a supersonic escape, was unable to remember anything that happened for about 20 seconds after operating the ejection equipment. He came down in the sea and had the good fortune to be picked up almost immediately by a target-towing tug. He was taken to a hospital, where it was found that he had a broken left arm, two black eyes, and a fractured pelvis.

Breast Feeding and Infection.—In the city of Dundee, almost two-thirds of the babies dying between the ages of 4 weeks and one year were artificially fed before they reached the age of one month, according to the city's health officer in his report for 1954. During the year, 2,967 babies were born in Dundee, of whom 370 (12.5%) were never breast fed, and only 22.8% were being breast fed at the age of 6 months. The number of deaths between the ages of 4 weeks and one year was 32. There were two deaths from gastroenteritis. One of these babies had never been breast fed and the other had been breast fed for two weeks. Of the 11 who died of pneumonia, only one was receiving breast milk when the illness developed.

Aid for Blind Physiotherapists.—To enable blind physiotherapists to give ultraviolet light therapy with the same accuracy and confidence as their more fortunate colleagues, an erythemameter has been designed to measure the degree of redness of a patient's skin. It consists of a photoelectric detector that communicates color to sound signals. A blind operator can thus tell by comparing nonirradiated and irradiated areas if his patient is in danger of receiving too much light. The apparatus was made by an electrical company in conjunction with the Royal National Institute for the Blind. The apparatus has been approved by a panel of the Chartered Society of Physiotherapy, and blind physiotherapists are to be trained in its use.

Death of Felix.—Arthur Felix, whose name is associated with the Weil-Felix reaction, died in London on Jan. 14. He was born in Poland in 1887 and while serving with the Austrian Army in World War I devised the diagnostic test for typhus. In 1921 he worked in Tel Aviv, Palestine, and in 1927 he accepted a position with the Lister Institute, London, where he remained until 1945, when he was appointed director of the International Enteric Reference Laboratory of the Public Health Laboratory Service, London. Much of Felix's work was concerned with the antigenic structure of bacteria, including the discovery of the Vi antigen of the typhoid bacillus and the rediscovery of O and H agglutination.

Hereditary Leptocytosis.—Hereditary leptocytosis, or Mediterranean anemia, characterized by Mongoloid facies, epicanthal folds, jaundice, splenomegaly, and hemolytic anemia, is limited largely to the Mediterranean region and is practically unknown in Great Britain. The presence of the disease in a Scottish family is reported by Israels and his colleagues (*Lancet* **2**:1318, 1955). Both parents were born in Scotland, and none of their ancestors were known to have originated outside this country. The mother, son, daughter, and a grandson suffered from the disease. All four were presumably heterozygous in respect to the thalassemic gene.

Ownership of Clinical Records.—A woman was charged with removing her clinical record from St. Mary's Hospital, London. She took the record from an office in the absence of the physician. This embarrassed the hospital authorities because the record covered a long and difficult case, in the course of which threats of legal proceedings had been made on several occasions. If a suit were brought they would need the clinical record as evidence. The magistrate ruled that a patient had no right to his or her hospital records, as they were the property of the hospital, and he ordered the patient to return it.

Glass-Topped Coffin for Earl.—The mummified body of the Earl of Bothwell, third husband of Mary, Queen of Scots, has "caught a chill" through lying for several centuries in the damp crypt of the Faarevejle village church. Experts at the National Museum in Copenhagen 60 miles away have dried it out and returned it in an airtight case with a glass lid. The Earl, accused of the murder of Mary's second husband, Lord Darnley, was imprisoned in Denmark for bigamy after fleeing from Scotland and died in prison in 1578. Tourists pay to see his mummified body, and a few years ago a British visitor noticed signs of decay. The Earl "recovered" after injections of penicillin.

Scottish Medical Journal.—A new journal, the *Scottish Medical Journal,* made its appearance in January. It is the journal of the Royal Medico-Chirurgical Society and of the Edinburgh Medico-Chirurgical Society and Obstetrical Society. It incorporates the *Edinburgh Medical Journal* and the *Glasgow Medical Journal,* founded respectively in 1805 and 1828. The journal, which is a monthly, is edited by Dr. Alexander Brown and will be devoted to original work in all branches of medicine, including the history of medicine.

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CORRESPONDENCE

PHYSICIANS IN SERVICE

To the Editor:—THE JOURNAL, alerted to the dangers facing American medicine, has aroused in us a keen interest in everything that affects the future practice of our chosen profession. For this reason, we cannot allow the article "The Civilian Doctor and Our Future Security," by Dr. Isador Ravdin (**159:** 1109 [Nov. 12] 1955), to go unchallenged. We are voluntarily serving our tour of duty with the armed forces and are presently assigned to an aircraft carrier with the Pacific fleet. Our experience in the Navy medical department has convinced us, quite as much as Dr. Ravdin is convinced, that a solution of the problems facing military medicine must be found. We are not convinced, though, that he, or many of the other leaders in military medicine, is aware of the real reasons why these problems exist. From discussions with medical officers in other branches of the service, we have learned that these are not exclusively problems of Navy medicine. There is real cause to feel that the medical forces are overstaffed and that physicians are poorly assigned. Recently, one of our patients returned from a Navy hospital after he had been kept there for two months following an operation for an inguinal hernia; another was there over a month before his surgery was even performed. Even a simple test such as the one for basal metabolism, which is usually done on an outpatient basis, required five days hospitalization for one of our patients. These incidents clearly show the extent to which the statistics of naval medicine are padded. We have seen many examples of qualified specialists languishing in small dispensaries or on ships where their talents are wasted; these are the men to whom the "Doctor-Draft" act was presumably aimed, so that their experience would be of value to us younger doctors. As long as dependent care is in the hands of the military medical departments, the families of servicemen will be unhappy and the physicians who render these services will be dissatisfied. We hear many complaints from the men of our ship about the assembly-line-type treatment their families have received in naval establishments. Many of them are already seeking treatment from private physicians, so that they may have the individualized attention and personal security that comes only through free choice in the selection of a doctor. The military has long complained that they are losing physicians because of the poor pay of service doctors in comparison with civilians; we do not feel that this is the primary reason that men are leaving the service but only an excuse. Most of us are leaving because of the slipshod way in which medicine is practiced in the Navy. Associated with this is the lackadaisical attitude toward the practice of medicine held by many of the career officers. All too often superior officers are superior in rank only and not in clinical acumen. It is remarkable that so few regular medical officers have availed themselves of the residency training offered by their own services; it follows that the doctor who ceases to learn ceases to be a good doctor. Many of these men admit that they chose a career in service medicine because it is less arduous than civilian practice; they prefer the 8 a. m. to 4 p. m. working day to night calls. We realize that these problems are much greater than can be understood by us in our narrow view of the over-all situation; we do know that our views are shared by nearly every other doctor we have talked to. Regardless of our feelings, we shall continue to provide the best medical care we can to our men, because of the habits ingrained in us by our civilian training.

LIEUT. ROBERT HAHN, M. C., U. S. N. R.
LIEUT. JOHN RAFFENSPERGER, M. C., U. S. N. R.
U. S. S. Hancock (CVA-19)
Fleet Post Office
San Francisco.

HIROSHIMA DIARY

To the Editor:—I read with pleasure the review of "Hiroshima Diary" on page 1801 of the Dec. 31, 1955, issue of THE JOURNAL. I certainly want to echo the sentiments of the reviewer. I had the privilege of knowing Dr. Michihiko Hachiya in 1945 and 1946. I was the surgeon of the corps that was responsible for the occupation of southwestern Honshu, with headquarters at Kure, a few miles from Hiroshima. Much of my time was devoted to the many medical problems related to the unfortunate city and its people. Dr. Hachiya was convalescing from his injuries, yet was making heroic efforts to reestablish and rebuild his hospital and was, at the same time, gaining as much medical knowledge of the effects of this awesome weapon as he could. Despite his grievous injuries, he worked like a man possessed; yet he was warm, friendly, and most helpful. I could never help but wonder how I would have reacted under the same circumstances. I was always impressed with the reverence with which his people held him. He was a man with a broken body amid thousands of casualties. Despite his personal problems, he provided leadership to his medical associates, which afforded the best medical care for patients in the face of most primitive conditions. He contributed his utmost to provide a haven for the sick and injured amid chaos. He is truly a great administrator as well as physician—a leader of men. Through his eyewitness account and his careful record of experiences of his friends, physicians can live in their minds the terrors of mass trauma. If they react as I did, they will wonder whether we have scratched the surface of the psychic problems associated with the weapon. They certainly will relive the awakenings of medical curiosity in the mind of a physician-victim. His breadth of understanding, vision, depth of compassion, and other attributes, for which we physicians pride ourselves, made us but as babes at the feet of this doctor. I can only add that every physician and medical student must read this book to be initially prepared for the holocaust that could face us at any time. Although this book deals with an unhappy subject, the beautiful prose of Dr. Hachiya has been retained in its original flavor throughout the superb translation.

COL. JOHN R. HALL JR., M. C.
Department of the Army
Office of the Surgeon General
Washington 25, D. C.

PARAVERTEBRAL INJECTION

To the Editor:—In the Dec. 31, 1955, issue of THE JOURNAL, page 1724, is an article "Intra-Articular and Paravertebral Injection of Cortisone in Osteoarthritis of Spine." I question the statement "Paravertebral injection of cervical vertebrae is relatively simple." Injection and infiltration of cervical paraspinal structures are potentially hazardous, and a lateral approach, as suggested by the authors, with the inadequate landmarks offered in the illustrations, should be seriously questioned. When a needle is inserted laterally "then advanced medially and anteriorly at a 45 degree angle until the transverse process is encountered and then directed toward the midline," two pitfalls may be encountered. Laterally, the vertebral artery may be pierced, and, medially, the ligamenta flava may be transfixed and the subarachnoid space entered, thus endangering the spinal cord.

ARTHUR M. PRUCE, M.D.
1447 Peachtree St. N. E.
Atlanta, Ga.

MEDICAL FILM REVIEWS

Fractures of the Forearm: 16 mm., color, sound, showing time 28 minutes. Produced in 1955 by Churchill Wexler Productions, Los Angeles, for and procurable on loan from Veterans Administration, Central Office Film Library, Washington 25, D. C.

This film discusses the displacing pulls of the forearm muscles and the potential effect of various fractures on the blood vessels and nerves in the area. The complex rotational relationship between the radius and ulna is described to emphasize the importance of accurate reduction to normal functioning of the hand. Typical forearm injuries, including fracture of both bones, fracture of the shaft of the radius, and fracture of the ulna with anterior dislocation of the head of the radius, are described. Methods of treatment are shown, and the problems of maintenance of reduction as well as of internal fixation are discussed. A section of the film is devoted to suggestions for the after-care of forearm fractures. The first portion of the film, devoted to the anatomic aspects of fracture of the forearm, is excellent, as is the section devoted to closed reduction and immobilization of the ulna with an intramedullary pin followed by reduction of the dislocation of the head of the radius. Some surgeons advocate reduction of the dislocated head of the radius before the ulna is immobilized rather than afterwards and would fix the ulna by a plate and screws rather than by an intramedullary pin. Although examples of plating and of bone grafting of fractures of the forearm are shown, the viewer is left with the impression that intramedullary fixation is preferable in most instances. Experience has shown that intramedullary fixation of fractures of the forearm may not be the procedure of choice and that other techniques may, in fact, be preferable. No mention is made of the difficult problem of comminuted fractures, and the frequent occurrence of nonunion in fractures of the ulna is not mentioned. The photography and narration are excellent. This film serves as a satisfactory introduction to the problems of fractures of the forearm and is particularly suitable for showing to fourth year medical students, interns, and physicians who occasionally treat such fractures.

BUSINESS PRACTICE

The American Medical Association and the Sears-Roebuck Foundation cooperatively have prepared a brochure entitled "A Planning Guide for Establishing Medical Practice Units." This publication contains practical suggestions on various phases of planning from selection of a site to arrangement of equipment and is available in the libraries of state and county medical society offices. From time to time parts of the brochure, slightly modified editorially, will be reproduced in the Business Practice section of THE JOURNAL.—ED.

MEDICAL FACILITIES

The eight basic elements of a medical facility are (1) reception room, control station, and business office; (2) waiting room; (3) consultation room; (4) examination and treatment room; (5) laboratory, including electrocardiograph and basal metabolism apparatus; (6) x-ray equipment; (7) toilet; and (8) utility and storage.

A medical practice facility can have no fixed, ideal plan. First, no two individuals or groups of individuals think alike or work alike. Second, the physical and geographic limitations that characterize a medical practice facility, whether for a new building, a remodeled building, or rented space, do not permit the adoption of any single plan. Each facility must be custom-made to express the individuality and to satisfy the working habits of those who will use it. The eight basic elements found in nearly all medical offices can be thought of as the "building blocks." While these eight elements may change in size and shape depending on methods of operation, they are always integrated in the medical practice facility, or their counterpart is conveniently available.

RECEPTION-BUSINESS OFFICE

The receptionist, who, in the small medical practice facility is also the doctor's assistant, the bookkeeper, and the bill collector, is the hub around which the office revolves. She should be so placed that she can keep an eye on all the workings of the office. She should see and acknowledge the arrival of the patient and must follow the progress of the doctor so that the patient flow has proper direction. If she discusses bills and appointments, the space should be large enough for others beside herself and private enough that her conversations are not generally overheard.

For the larger office the functions mentioned above may be split among two, three, or even more persons. The receptionist still should be able to see the entrance and the waiting room. If she is too far removed to watch the progress of the doctor, she has to be informed by the nurse assistant of this progress so she can keep the flow of patients coming. If there is a separate business manager–bookkeeper, a private space should be provided for working on records and discussing bills with patients. It is advisable that this office be located so that it is accessible to outgoing patients. The exit from this office should permit patients to leave without backtracking, or going through the waiting room. Proper relationship to the entrance will also assist in the control of deliveries to the office.

RECEPTION-WAITING ROOM

Your patients receive their first impression from your waiting room. Its appearance may indicate the type of care they can expect to receive. A wait in a crowded, out-of-date room can depress and disgruntle even the best and steadiest of patients. The chairs, tables, and lamps should be adequate in number and well spaced so as to make reading possible and to give the patients a feeling of freedom. Your own patient load provides the only criterion for the number of chairs you must provide. If your schedule is always well maintained, you need only a minimum. If you are burdened with emergency calls and extended house or hospital calls, then the waiting room should be more ample. Needless to say, some thought should be given to decoration: the walls, upholstery, pictures, and drapes. Tasteful, harmonizing colors that are cheery rather than drab are desirable. The over-all effect should be one that is home-like and restful.

The waiting room preferably should permit a view of the outside and, if possible, the view should be a pleasing one. Flowers, trees, or distance are the best, but when this is impossible an interesting view of people and activity is the second choice. The waiting room should be removed from the actual office activity. It should not be a thoroughfare for traffic, nor should it be an office for the discussion of bills and appointments between the receptionist or office manager and patients. If one enters the office directly from the out-of-doors, it is well to have a lobby to prevent drafts. If the business office opens on the lobby, it may well serve to receive the incomer and to determine his business. This, in turn, allows some to be directed to the waiting room and others to be taken directly to the doctor without incurring hurt feelings and arguments.

CONSULTATION ROOM

The consultation room is usually the stopping point, at some time, for all patients passing through the office. The patient is usually sent there for discussion of symptoms and progress and simple examinations. He is then sent to an examination or treatment room, from which he may return to the consultation room for further discussion and prescription. However, there seems to be a trend to simplify and speed up this procedure by concentrating the entire visit of the majority of the patients to the examination room, with the consultation room used more as a private retreat and for discussion of more serious cases. This allows the doctor to dispense with much of the bother of odd examination paraphernalia and to develop the

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consultation room as a place for reading and relaxation. This can have a salutary effect on both patient and doctor. Comfortable chairs, even a place to stretch out and relax, can increase the doctor's efficiency and relieve his tension. The air of relaxation in this room can also help put the patient in a better frame of mind to accept the doctor's diagnosis. Ample space to prevent a cramped, closed-in feeling and a pleasant view are desirable. Tasteful colors, drapes, pictures, and furniture are necessary.

EXAMINING-TREATMENT ROOM

It is in the examining-treating room, with its variations, that the doctor usually has his closest contact with the patient. This is his work room. It needs, first of all, to be efficient. In other words, it should be properly and adequately lighted, with all the equipment necessary placed in such a way as to permit the doctor and his assistants to work rapidly and easily. Here space cannot be wasted; neither can it be reduced beyond a certain minimum. Unnecessary steps must be eliminated; yet there should be room to move around easily and without interference. This is one room where the needs and the working habits of the doctor must be investigated carefully and thoroughly so that he may have what best meets his needs and desires. While he has been trained to do many things well, despite adverse conditions and scanty equipment, there is no need to handicap him on his home ground.

Seldom is one examination or treatment room enough. Two rooms can often more than double the doctor's capacity, and some doctors have as many as eight. Where there are several rooms, patients can be prepared ahead of time by the assistants. Furthermore, a number of procedures can be handled by the assistants, on direction of the doctor, while he is putting his time to better use with other patients. When this practice is followed intelligently and does not slip into an impersonal production-line technique, it results in increased efficiency.

When the examination-treatment room is used for most of the doctor-patient contacts, it is necessary to provide a few things not formerly found there. It is also necessary to provide for the patients' comfort and convenience. For the doctor, a desk or writing space, and perhaps a satisfactory chair for use during discussions with the patient, may be ample additions. For the patient, a cubicle with dressing facilities, mirror, clothes

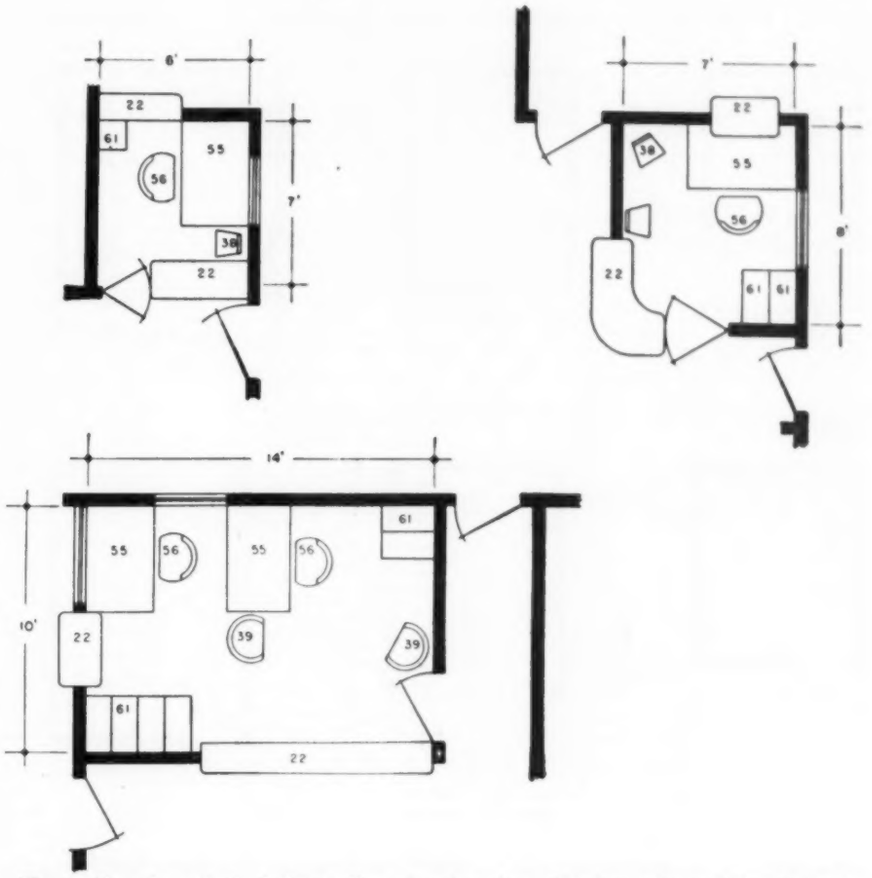

Fig. 1.—Plans for reception-business offices of various sizes. (Numbers refer to equipment list in original booklet.)

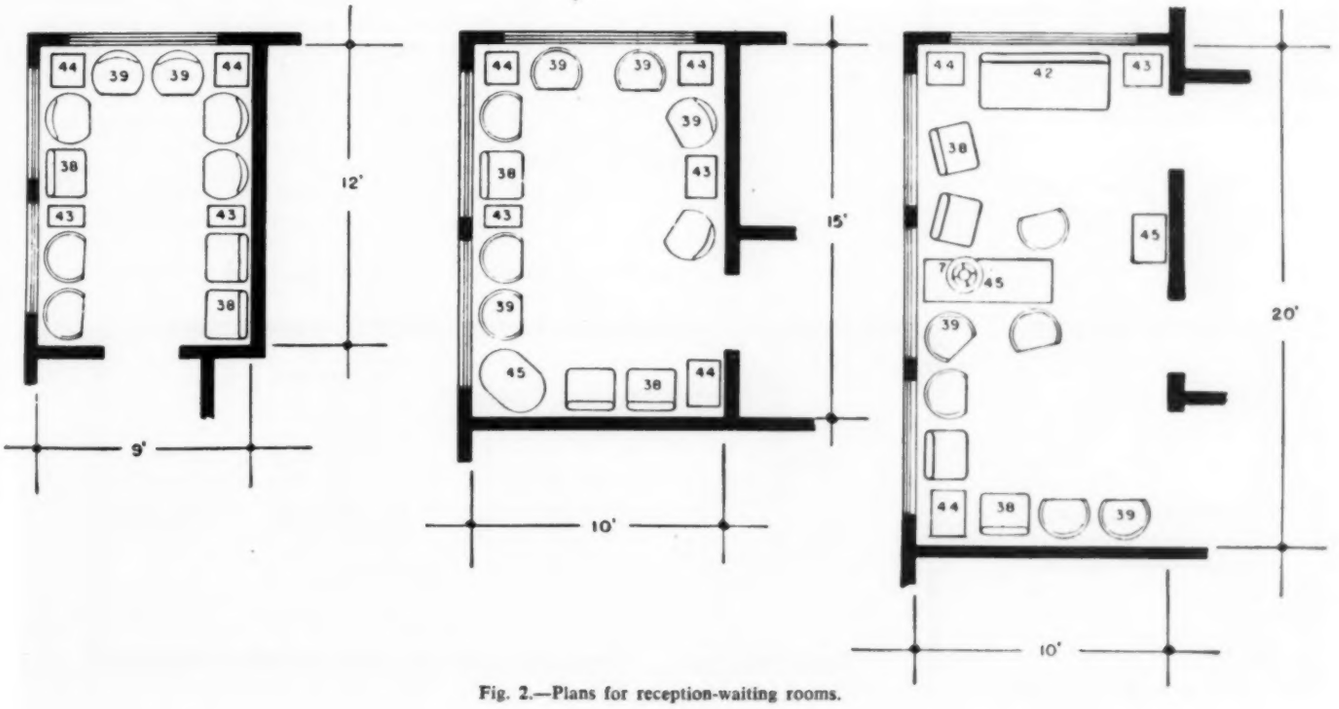

Fig. 2.—Plans for reception-waiting rooms.

hooks, slippers, chairs, or low bench in or immediately adjacent to the examination-treatment room is a great convenience. A comfortable chair, magazines, and ash tray are also advisable to ease the patients' waiting time when the doctor is delayed with some other patient.

LABORATORY

The laboratory varies from a few shelves, sink, sterilizer, and such equipment in the corner of the examination room to a complete laboratory in a separate room. In the smaller office it is best combined with other uses for the saving of space and of steps. The nurses' work room, the store room, the recovery room, and a spare examination room are all possible elements that can, under certain conditions, be combined with the laboratory. The ideal, of course, is a room designed for specific laboratory procedures with adequate equipment and supplies. However, the extent to which each doctor desires to carry on his own procedures determines the extent to which this ideal is approached.

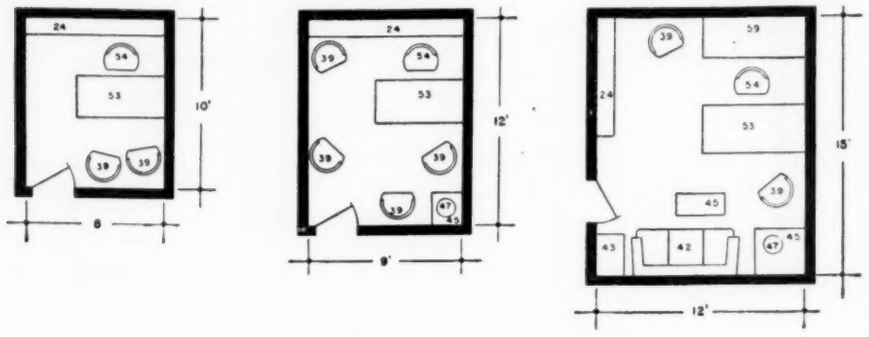

Fig. 3.—Plans for consultation rooms.

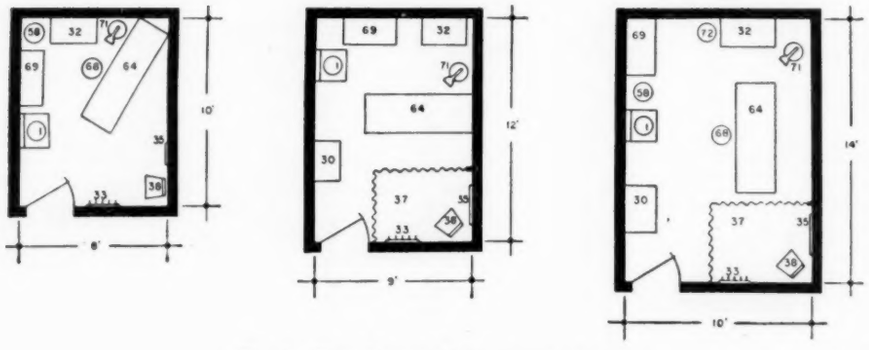

Fig. 4.—Plans for examining-treatment rooms.

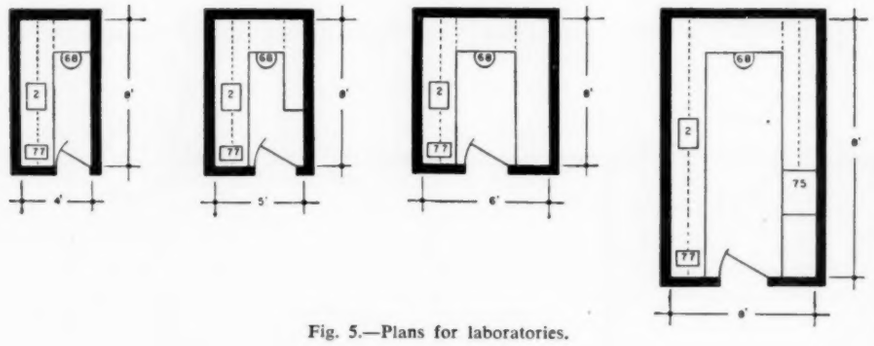

Fig. 5.—Plans for laboratories.

RADIOLOGICAL UNIT

Many doctors, because of either location or their type of practice, find x-ray equipment helpful or necessary. This may range from a very small and simple setup to a complete diagnostic radiological facility. A fluoroscope is probably the minimum in such equipment and is the least demanding in space requirements. Room for the machine, doctor, and patient, with a minimum additional area for service and adjustment, requires a minimum of 48 sq. ft. Best situated in an inside room by itself, the fluoroscope can also be in the corner or at one end of an outside examination room if means are provided for darkening. Dressing facilities are also advisable.

Space for other radiological units has to be determined on the basis of each additional unit. As the size and/or use of the radiographic unit increases, the need for adjacent space increases. Dark rooms, dressing rooms and storage space for films all have to be increased. The necessity for x-ray protection also increases. Concrete, lead-lined, or marble-covered walls have to be provided, and, when floors above and below are inhabited, the ceiling and floor also should be protected.

UTILITY, STORAGE, TOILETS

Every office must have space to be used for storage or for utilitarian services not necessarily connected with the practice of medicine but necessary for the operation of the facility. This includes work rooms, closets, storage shelves or rooms for supplies, and room for boiler or air-conditioning equipment. Despite the fact that it may at first be neglected in the office plan, space for some of these uses will have to be included. The office in its own building will have to provide space for heating and air conditioning in addition to storage and work space. The office in a building where other tenants already have offices may have to provide only space for air conditioning and storage, while the tenant of a modern air conditioned building will have to think only of his storage and work areas.

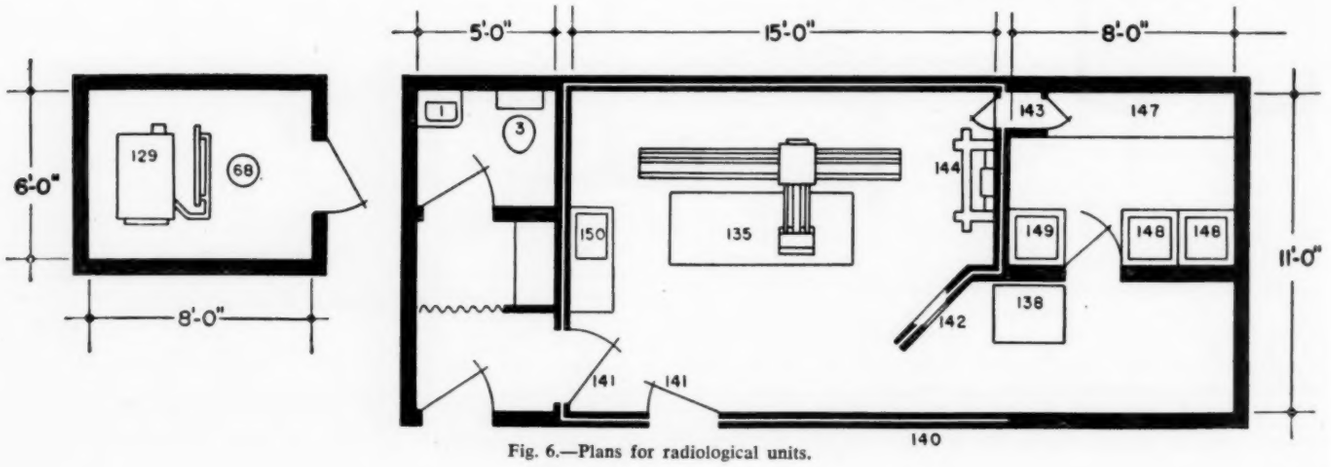

Fig. 6.—Plans for radiological units.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Ten-Year Prognosis of Acute Myocardial Infarction. M. M. Weiss. Am. J. M. Sc. **231:**9-12 (Jan.) 1956 [Philadelphia].

This report is concerned with a follow-up of 211 patients who lived more than two months after their first myocardial infarction. A survival period of two months was selected because by this time the majority of patients who will live have become ambulatory and are usually ready to resume a modified or regular routine of life. Only patients with characteristic clinical and electrocardiographic evidence were selected. There are patients with a slowly progressive coronary artery disease who must have had a myocardial infarction, but the date of the infarction cannot be determined. They were excluded from the study. Seventy-seven or 36.5% of the patients lived more than 10 years. The majority of those who died did so in the first five years. More young people live more than 10 years after an infarction than do those in the older age groups. The patient who has made a good functional recovery lives longer than those who are disabled by congestive heart failure, anginal syndrome, or a cerebral embolism. In general, economic rehabilitation paralleled the functional cardiac status, but some patients returned to their former occupations despite the presence of the anginal syndrome or symptoms of congestive heart failure. The work status of all the patients naturally altered as they became older, had another myocardial infarction, or manifested such complications as the anginal syndrome or congestive heart failure. In this report, 76% of the 60 men who survived a decade were still at work. Others were able to work but had elected to retire. The major cause of death was cardiovascular disease, accounting for 88% of the deaths.

Clinical Evaluation of the Use of a Rectal Mercurial Diuretic in Patients with Chronic Congestive Heart Failure. N. Makous, P. Jennings, E. H. Funk Jr. and J. B. Vander Veer. Am. J. M. Sc. **231:**86-91 (Jan.) 1956 [Philadelphia].

Self-administration remains a problem in therapy with mercurial diuretics in spite of the availability of preparations for subcutaneous and oral administration, because there are patients in whom neither of these is satisfactory due to inconvenience or side-reactions. Mercaptomerin (Thiomerin) sodium has recently been made available in suppository form. The authors evaluated this form of mercurial diuretic in 23 patients with chronic congestive failure who were receiving digitalis and had been receiving mercurial diuretics parenterally for at least three months prior to the study. These patients were selected from a large group attending the Cardiac Clinic of the Pennsylvania Hospital. Their heart diseases were of arteriosclerotic, hypertensive, rheumatic, syphilitic, or congenital type. The effectiveness of suppository therapy was determined by the clinical findings and by comparison with the number of weekly injections of mercurials required before, during, and after use of the suppository. An average of approximately one suppository a day reduced the requirement of parenterally given mercurials by more than half. Nineteen of the 23 required less than one injection weekly while using suppositories, 14 required less than one monthly, and 9 required no parenterally given mercury. In contrast to mersalyl (Salyrgan) and mercurin (Mercuzan), and like meralluride (Mercuhydrin), the suppository form of mercaptomerin does not appear to have local toxic or irritative effects. In this study, none of the patients showed either subjective or objective evidence of rectal irritation, in spite of prolonged use. The authors conclude that mercaptomerin (Thiomerin) suppositories are effective in reducing or eliminating the need for parenterally administered mercury in many patients with chronic congestive heart failure.

Contribution to the Study of Tumors in the Aberrant Thyroid. C. Sabbatini. Riforma med. **69:**1350-1358 (Nov. 26) 1955 (In Italian) [Naples, Italy].

The occurrence of multiple tumors in aberrant thyroid tissue in the anterior region of the neck is reported in a 44-year-old man and a 66-year-old woman. Clinical and operative examination revealed a normal thyroid in both patients. The tumors were removed surgically, and histological studies revealed benign papillary cystadenomas in the first patient and thyroidal adenomas with signs of probable malignant changes in the second. Two years after the intervention, the local and general condition of the first patient was excellent. Examination of the thyroid and the nearby lymph nodes did not reveal changes in their volume and consistency. A follow-up of the second patient one year after the operation revealed that she too was in good health. The only finding on examination of the neck was the presence of a slight scar. On the basis of the results in his two patients and of those reported in the literature, the author makes a distinction between histologically and clinically malignant tumors of aberrant thyroid tissue. The fact that the removal of such tumors is followed by a long survival (more than 15 years in some instances) of the patient in good health and that during their growth recurrent tumors of aberrant thyroid tissue have never caused changes of the infiltrating type in the adjacent tissues, as is regularly observed in recurrences of the common malignant tumors, would seem to support Sabbatini's concept that this kind of tumor is not malignant. He believes that what has been up to now thought to be a recurrent tumor of aberrant thyroid tissue is only the development of other aberrant thyroidal foci in the same location from which the primary tumor was removed. These new foci have the same characteristics as the first tumor but are entirely independent of it.

Goiter from Prolonged Ingestion of Iodide. H. H. Turner and R. B. Howard. J. Clin. Endocrinol. **16:**141-145 (Jan.) 1956 [Springfield, Ill.].

This report is concerned with the development of myxedema and/or goiter after the administration of iodide as syrup of hydriodic acid, potassium iodide, or Lugol's solution for two to five years to asthmatic patients. There were seven males and six females, ranging in age from 5 to 17 years. All had enlargement of the thyroid varying from grade 2 to grade 5, and in seven there were laboratory and clinical findings consistent with myxedema. The cessation of iodide therapy and the administration of desiccated thyroid or sodium l-thyroxine resulted in disappearance of the myxedema and regression of the goiter to normal or almost normal size in each patient. One of the three representative case reports concerned a boy, aged 7½ years, who was first seen in March, 1954, because of a tumor in the neck of three months' duration. The patient had had asthma all of his life and had been taking syrup of hydriodic acid (¾ teaspoon twice daily) for the preceding five years. The thyroid was diffusely enlarged (about grade 3), smooth, and firm. The circumference of the neck was 26 cm. Administration of iodide was discontinued, and ½ grain of desiccated thyroid daily was prescribed. At the end of one month the dose was increased to 1 grain daily. After six months the child had gained 2 lb. and had grown 2.5 in. The gland

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The place of publication of the periodicals appears in brackets preceding each abstract.

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had regressed to grade 1 status. After one year of thyroid therapy, his weight and height had further increased and the size of the thyroid and circumference of the neck had further decreased. Treatment with desiccated thyroid was then discontinued. The activity of the thyroid in 5 of the 13 patients was evaluated by the ability of the gland to accumulate I^{131}. The tests were carried out on two patients before administration of iodide was stopped. Their thyroids showed a low uptake of I^{131}, typical of that seen during iodide therapy. On the other hand, the thyroidal uptake in the patients no longer receiving iodides approached that of normal persons. It appears that an excess as well as a lack of iodide will result in a diminished production of hormone by the thyroid. The excess supply of iodide apparently interferes with the mechanism for the synthesis of the thyroid hormone. Although the incidence of myxedema and/or goiter is small among the great numbers of asthmatics and others who take iodides without interruption for prolonged periods, it is greater than in the general population. From the evidence available at present, it is concluded that in some individuals prolonged iodide therapy may have an antithyroid action similar to that of thiouracil.

The Anemia of Infection: 20. The Kinetics of Iron Metabolism in the Anemia Associated with Chronic Infection. J. A. Bush, H. Ashenbrucker, G. E. Cartwright and M. M. Wintrobe. J. Clin. Invest. **35**:89-97 (Jan.) 1956 [New York].

Bush and associates point out that a method has been developed for the determination of the turnover rate of iron through the plasma and red blood cells. The use of these rates makes it possible to understand better the alterations in the kinetics of iron metabolism that occur in various anemias. In addition, an estimation of the life span of the red blood cells can be obtained. The authors present studies on six patients with anemia of chronic infection and on 10 normal subjects. The normal subjects were healthy young males. The patients were men ranging in age from 33 to 65 years, of whom one had silicotuberculosis with secondary aspergillosis, another tuberculosis (osseous and pulmonary), a third chronic lymphangitis and cellulitis of the right leg, a fourth unresolved pneumonia, a fifth severe tuberculosis (pulmonary), and the sixth tuberculous pneumonia. The radioactive iron used was supplied as ferric (Fe^{59}) chloride on allocation from the U. S. Atomic Energy Commission. Ferric chloride, containing 3 to 6 mcg. of iron and 5 to 20 μc of radioactivity, was buffered to pH 6.0 with 4% sodium citrate and incubated for 30 minutes at room temperature with 12 ml. of the subject's own plasma. Ten milliliters of this material was injected intravenously at 9:00 a. m. after the subjects had eaten. Plasma samples were obtained at 15-to-30-minute intervals after the injection until the activity in 1 ml. of plasma had decreased to twice the background count. Body surface counts were made with a mobile scintillation counter over the liver, spleen, and sacral bone marrow sites in two patients and in two control subjects. The average half time of plasma Fe^{59} disappearance in the patients was 0.51 hours as compared with 1.39 hours in the control subjects. The average plasma iron turnover rate and red blood cell iron turnover rate in the patients were 0.61 mg. per kilogram per day and 0.58 mg. per kilogram per day, respectively, as compared with 0.56 mg. per kilogram per day and 0.52 mg. per kilogram per day in the normal subjects. The incorporation of Fe^{59} into the red blood cells of the patients was initially more rapid than in the control subjects. The ultimate percentage of injected Fe^{59} incorporated into erythrocytes was the same in both groups. The average "apparent" erythrocyte life span, as calculated from the above data, was significantly shorter in the patients than in the control subjects. The body surface counting patterns of uptake and delivery of Fe^{59} by the liver, spleen, and bone marrow in the patients with infection did not differ significantly from those in the normal subjects. Very little activity entered the liver or spleen. These data suggest that the erythrocyte life span in patients with chronic infection is shortened. The bone marrow is unable to compensate for this modest shortening of the erythrocyte life span. When consideration is given to the fact that a normal marrow is capable of increasing its production sixfold to eightfold, it is clear that there is marked inhibition of erythropoiesis in such patients.

Dietetic Treatment of Peptic Ulcer. R. Doll, P. Friedlander and F. Pygott. Lancet **1**:5-9 (Jan. 7) 1956 [London, England].

The present investigation was planned as a controlled trial of certain types of diets. The value of dietetic treatment of peptic ulcer was assessed in 64 inpatients with gastric ulcers, 80 outpatients with gastric ulcers, and 50 outpatients with duodenal ulcers. The inpatients were divided into two equal groups; patients in one group were given the standard hospital ulcer diet, while in the other they were given an almost normal diet. As compared to patients on the standard hospital ulcer diet, those on the almost normal diet showed a slightly but statistically insignificantly higher rate of healing of ulcers and a significantly higher weight gain; also, an appreciably higher proportion reported themselves completely free of pain throughout treatment. The outpatients were advised either to continue for a year on the standard ulcer diet with which they had previously been treated or to revert to a wholly normal diet. At the end of a year, the proportion of patients who had remained free of pain and in whom the ulcer was radiographically healed was practically the same in the two groups. The authors conclude that dieting with bland foods does not increase the rate of healing of peptic ulcers.

The Hospital Staphylococcus: A Comparison of Nasal and Faecal Carrier States. J. Brodie, M. R. Kerr and R. Sommerville. Lancet **1**:19-20 (Jan. 7) 1956 [London, England].

It is widely held that the nasal carrier is the main source of infection in micrococcic (staphylococcic) disease acquired in the hospital. The authors draw attention to the intestinal carrier as a potential source of micrococcic infection. They resorted to serological rather than to phage-typing of micrococci. Phage-typing is time-consuming, and serological typing as used in the present studies is within the scope of the clinical pathologist. The only special requirement is the preparation and issue of standard antiserums. The search for intestinal carriers was based on isolations from rectal swabs. The fact that the source of these strains was the feces, and not the skin of the buttocks, was confirmed by a series of comparative tests of the nose, skin, and feces. The simultaneous search for nasal and intestinal carriers was made in two dysentery wards in which there was an outbreak of micrococcic disease at the time of the survey. A table compares the findings of the carrier status at the start of the survey with that of patients on admission and after one week's residence in the hospital. This table includes the results for nasal and fecal strains. Analysis of micrococci by serological typing and sensitivity testing demonstrated that the proportion of Micrococcus carriers in the general community (new admissions to the hospital) differed from that in a hospital community. The general carrier rate was doubled as a result of hospitalization. The number of nasal carriers of one of the serotypes increased fourfold (from 6 to 27%), while intestinal carriers increased sevenfold (from 5 to 35%). The results obtained by antibiotic-sensitivity testing of the same serotype confirmed the general experience that one week's residence in the hospital was associated with a high frequency of infection with cross resistant strains. All strains isolated from patients after one week in the ward were sensitive to erythromycin. Of 63 patients, 50 were nasal and intestinal carriers at the same time. Of these 50, 43 were carrying the above-mentioned serotype. The resistance patterns of these strains differed. Some nasal and fecal strains showed the same resistance patterns, but in one group of 15 patients the fecal strains were resistant to chloramphenicol and five other antibiotics whereas the nasal strains, although resistant to the five antibiotics, were sensitive to chloramphenicol. In the hospital the intestinal carrier of micrococci, especially one certain serotype, seems to play a more important part in communicating micrococcic disease than has been realized.

Primary Aldosteronism, A New Clinical Entity. J. W. Conn and L. H. Louis. Ann. Int. Med. **44**:1-15 (Jan.) 1956 [Lancaster, Pa.].

The term "primary aldosteronism" was coined by the authors for a new clinical syndrome that was observed in a 34-year-old woman with a disease formerly called "potassium-losing nephritis" in whom an extensive metabolic balance study was

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carried out for one year. The patient stated that for seven years she had been having attacks of intense generalized muscular weakness resulting occasionally in complete "paralysis" of both lower extremities. She complained of frequent attacks of "spasms of the muscles" that were typical of tetany, involving mainly the upper extremities, but occasionally also the lower extremities. Examination revealed well-developed muscles; blood pressure was 176/104 mm. Hg; the size of the heart was normal; there was no edema; Chvostek's and Trousseau's signs were positive; and there was hyperactivity of all tendon reflexes. Initial laboratory values revealed a hypernatremic, hypopotassemic alkalosis with marked elevation of blood pH and of carbon dioxide combining power, associated with alkaline urine. The major functional defect consisted of hyposthenuria unaffected by administration of β-hypophamine (Pitressin) tannate. The muscular weakness could be explained by the hypopotassemia and the tetany by the severe alkalosis. The patient obviously did not have adrenal cortical hyperfunction (Cushing's syndrome), since eosinophils and 17-hydroxycorticoids were normal. Urinary 17-ketosteroids were always normal. Assays of urine for sodium-retaining corticoid, presumably aldosterone, gave values from 4 to 30 times greater than those found in the urine of normal adults. There was great resistance to several attempts at repletion of potassium with as much as 300 mEq. of potassium per day. There was significant but short-lived retention of potassium, accompanied by loss of sodium. On cessation of administration of supplementary potassium there ensued abrupt retention of sodium and loss of potassium. On surgical intervention a cortical adenoma, 4 cm. in diameter, arising from the right adrenal gland was observed. A right adrenalectomy was performed and the contralateral adrenal, which appeared to be grossly normal, was left in its normal position after a wedge biopsy that revealed an atrophy of the fascicular zone of the cortex had been obtained. Bioassays for sodium-retaining corticoid carried out on extracts of the removed tumor tissue revealed that the tumor tissue contained 100 to 200 times as much aldosterone as does beef adrenal, 10 times as much as hog adrenal, and 30 times as much as was found by Wettstein in an adrenal tumor that had produced adrenal cortical hyperfunction. Postoperative metabolic balance studies for 112 days revealed that sodium and potassium equilibrium continued, blood pressure remained normal, and proteinuria had not recurred. Blood pH, carbon dioxide combining power, and serum sodium and potassium levels continued to be normal. Daily determinations of 17-hydroxycorticoids, 17-ketosteroids, and circulating eosinophils remained normal, as they were preoperatively. Patients with such clinical and laboratory manifestations as those observed in this patient should be subjected to adrenalectomy. Twelve additional cases in which an adrenal cortical adenoma was disclosed at surgical intervention or at autopsy have been reported by other workers; nine of the patients were cured of primary aldosteronism by surgical removal of the adenoma, and in the other three the condition was recognized at autopsy.

Observations on the Use of Prednisone in Patients with Progressive Systemic Sclerosis (Diffuse Scleroderma). G. P. Rodnan, R. L. Black, A. J. Bollet and J. J. Bunim. Ann. Int. Med. 44:16-29 (Jan.) 1956 [Lancaster, Pa.].

Prednisone was given orally to six patients with progressive systemic sclerosis (diffuse scleroderma). Administration of 20 to 30 mg. of the drug daily, in divided doses, was continued for uninterrupted periods of up to four and one-half months. In all patients the skin conditions improved, with diminution in hyperpigmentation, swelling, and tightness. Improvement began about one week after the institution of the treatment. Prednisone showed potent antirheumatic activity in two patients with joint involvement; relief of pain, tenderness, and swelling resulted within one day of therapy. One patient with pulmonary involvement obtained considerable symptomatic relief, with improvement in ventilatory capacity. Gastrointestinal manifestations were not lessened. Inflammatory changes in the synovial tissue persisted. In all patients the sedimentation rate was reduced and the C-reactive protein, when present before treatment, disappeared. Only slight changes were noted in the concentration of the serum protein fractions. The hematocrit value increased in one patient. Undesirable side-effects of prednisone were minimal.

Adrenocorticotropin and Cortisone in the Treatment of Severe Reiter's Syndrome. D. T. Foxworthy, R. M. Poske, E. M. Barton and others. Ann. Int. Med. 44:52-62 (Jan.) 1956 [Lancaster, Pa.].

Corticotropin (ACTH) and cortisone were given to 10 patients with Reiter's syndrome admitted to the Veterans Administration Hospital, Hines, Ill., in whom symptoms were not controlled by analgesics and other conservative measures. Six patients had the classic triad of urethritis, conjunctivitis, and migratory polyarthritis. Two patients did not have urethritis, and two others did not have conjunctivitis, but these four had typical perimeatal erosions and balanitis circinata, and two of them also had lesions on the oral mucous membrane. The total dose of corticotropin administered varied from 2.152 to 3.910 gm., that of purified corticotropin gel from 0.470 to 1.435 gm., and that of cortisone from 0.350 to 9.580 gm. The duration of therapy varied from 14 to 87 days and averaged 62 days in the eight adequately treated patients. Both corticotropin and cortisone, when given in adequate doses for a long enough period, were effective in suppressing symptoms. Three patients received injections of 25 mg. of hydrocortisone into single joints in which effusion persisted; in each of them it was effective in suppressing the inflammation. The course of the disease was not shortened by the hormone therapy. Secondary infections did not occur, and there were no associated systemic infections during or immediately after steroid therapy. While not curative, corticotropin and cortisone are the most valuable agents now available to relieve pain, increase the patient's appetite, and prevent the excessive weight loss, muscle atrophy, and debility usually seen in patients with the severe form of Reiter's syndrome. Large suppressive doses of the hormone should be given early and should be gradually reduced to smaller maintenance doses and discontinued when the symptoms and findings have apparently subsided. A recurrence of symptoms at any time is an indication to increase the dose or to reinstitute treatment. Prolonged therapy may be needed. Treatment with the hormones is considered unnecessary in the milder form or late in the course of the disease.

Pulmonary Edema and Pulmonary Fibrosis in Malignant Hypertension During Treatment with Ganglion-Blocking Agents. H. J. Viersma. Nederl. tijdschr. geneesk. 99:3593-3603 (Nov. 26) 1955 (In Dutch) [Haarlem, Netherlands].

Viersma reports observations on three patients with malignant hypertension and renal insufficiency who at first had shown improvement during treatment with a salt-free and low-protein diet combined with the administration of a methonium compound (hexamethonium chloride). Pulmonary edema developed insidiously, and in two patients this progressed to interstitial and intra-alveolar pulmonary fibrosis. Death from asphyxiation followed in these patients. Reports by several observers show that these different groups of patients all have a malignant or a premalignant hypertension together with disturbances in the renal function and that they received methonium compounds or other blood pressure–reducing agents. The clinical picture of insidious pulmonary edema is also observed in other conditions such as the so-called uremic pulmonary edema. The author suggests that in renal insufficiency certain conditions may favor the retention of fluid in some of the pulmonary capillaries, probably by slow exudation of edema fluid that has a high protein and fibrin content; as a result, the blood stagnates and fluid accumulates first in the interstitium and then even more markedly in the alveoli. This type of pulmonary edema differs from the syndrome of acute pulmonary edema. It is suggested that methonium compounds might be an indirect cause of this condition. Careful supervision is therefore vitally important during treatment with these ganglion-blocking agents. Lassitude, anorexia, dyspnea, tachycardia, and moderate increases in temperature are early symptoms of this threatening complication and should induce the physician to resort to roentgen examination of the lungs. Dehydrating treatment should be instituted at once if signs of fluid accumulation appear in the lungs. This can be done by the administration of from 200 to 400 cc. of 20 to 50%

solutions of magnesium sulfate or sodium sulfate, or, if vomiting that cannot be controlled by chlorpromazine should occur, by rectal administration of 100 cc. of the same solutions four times daily. In serious cases, peritoneal lavage should be carried out with a solution that has been made hypertonic by the addition of glucose. Cardiac insufficiency may have to be counteracted by administration of digitalis.

Hand-Schüller-Christian Disease: Report of a Case with Unusual Lung Changes. R. S. McNeill and H. MacD. Cameron. Thorax **10**:314-320 (Dec.) 1955 [London, England].

In the case of Hand-Schüller-Christian disease described in this paper, superficial and mediastinal lesions were found in bone, lung, and lymph nodes. Until recently, Hand-Schüller-Christian disease was considered to be a disturbance of the lipid metabolism and was included in the group of xanthomatoses along with Gaucher's and Niemann-Pick disease. It is now considered to be a primary reticuloendotheliosis or histiocytosis in which the histiocytic cells may become secondarily infiltrated with fat. Exophthalmos, bony defects in the skull, and diabetes insipidus were for a time regarded as the classic signs of the disease. However, it is now recognized that the lesions may appear wherever reticuloendothelial tissue is encountered. Christian's triad is not a *sine qua non* of the diagnosis, and the disease can occur without any cranial lesion at all. The recognition of a relationship between eosinophil granuloma and Hand-Schüller-Christian disease has resulted mainly from the observation of conditions intermediate between the solitary bony lesion of the former and the fully developed picture of the latter disease. The distinction between the two conditions is based on the distribution of the lesions; thus patients with Hand-Schüller-Christian disease show widely distributed lesions, whereas eosinophil granuloma is localized to bone and frequently results in a single lesion. Since the pulmonary lesions of Hand-Schüller-Christian disease are readily detected by radiography, they are among those most frequently described. The pulmonary lesions usually consist of diffuse bilateral infiltrations, nodular or linear, that progress to give the radiological picture of pulmonary fibrosis. This, in turn, is followed by a diffuse cystic change giving the radiological appearance of "honeycomb lung." In the 30-year-old man whose history is presented, the radiological changes in the lungs were curiously different from those described by other writers. There were large patches of infiltration with cavitation that were presumably caused by the evacuation of necrotic tissue, because xanthomatous cells were found in the sputum. These radiological changes in the lung closely resembled tuberculosis, and the large paratracheal lymph node mass could well have been interpreted as tuberculous adenitis. A swelling in the neck was incised and some tissue removed by curettage five months after its appearance. Histological examination suggested a reticulosis, but its nature was not clear. Two months later, a series of roentgen irradiations was begun, and a dose of 3,000 r was given in three weeks. When similar swellings appeared at costochondral junctions, excised tissue was diagnosed as eosinophil granuloma. Repeated roentgen irradiations, which seemed to have some suppressive effect, and, as a last resort, a trial with Urethane, did not prevent death, which occurred 26 months after the first appearance of the swelling in the neck.

Prevention of Experimental Tuberculosis with Isoniazid. S. H. Ferebee and C. E. Palmer. Am. Rev. Tuberc. **73**:1-18 (Jan.) 1956 [New York].

Twelve hundred and twenty-four young guinea pigs were separated into five comparable groups. Three groups of the animals received isoniazid in average daily doses of 1, 5, and 25 mg. per kilogram of body weight, respectively, in their drinking water. The drinking water of the remaining two groups did not contain isoniazid. One month after administration of the drug had been started, animals in the three groups that received isoniazid, as well as those in a control group, were given a large intraperitoneal challenge of virulent tubercle bacilli. The fifth group of animals, designated as normal, also did not receive the drug and were given only a placebo instead of the virulent challenge. Ten weeks after the challenge, isoniazid administration was discontinued for a randomly selected part of the surviving members of each group that had received the drug. Fourteen weeks after the first virulent infection, this selected group of animals and those still under treatment with isoniazid were subjected to a second virulent infection. Results showed that a daily dose of as much as 5 mg. of isoniazid per kilogram of body weight, if started before the challenge infection and continued for only 10 weeks after the challenge, is apparently sufficient to prevent mortality from tuberculosis for at least the 26 weeks observed in the experiment and to allow the guinea pigs to grow in weight at the same rate as normal, untreated uninfected guinea pigs. It also appeared that after an isoniazid-treated tuberculous infection, guinea pigs responded to a later, untreated tuberculous infection very much as they do after vaccination with BCG.

Clinical Aspects and Therapy of Abdominal Tuberculosis During Childhood with Special Consideration of Roentgenologic Examinations. J. K. Dittrich and L. Weingärtner. Beitr. Klin. Tuberk. **115**:1-26 (No. 1) 1955 (In German) [Berlin, Germany].

The authors include in the concept of abdominal tuberculosis processes that involve the peritoneum or organs within the peritoneum, but not urogenital tuberculosis. Abdominal tuberculosis in children is usually caused by the bovine type of tubercle bacillus. The pathological and anatomic aspects are discussed on the basis of the literature and of the results of autopsies in 70 cases; the clinical aspects on the basis of observations in 239 patients. Three different forms of abdominal tuberculosis are differentiated: peritoneal tuberculosis, which may be either exudative or adhesive in type; tuberculosis of the mesenteric lymph nodes; and true intestinal tuberculosis. Abdominal tuberculosis frequently remains unrecognized for a considerable period of time. The outcome of tuberculin tests is generally weak or completely negative. Whereas roentgenologic examination is of primary importance in the diagnosis of pulmonary tuberculosis, it is generally assumed that in abdominal tuberculosis, particularly that occurring during childhood, roentgenologic examination is of little value. The authors, however, demonstrate the great value of this examination. In order to detect tuberculosis of the mesenteric lymph nodes, roentgen examination without the use of contrast medium is employed first. The roentgen shadow of calcified mesenteric lymph nodes appears granular and not homogeneous. Tuberculous lymph nodes that have not become calcified can often be recognized either by creating a difference in shadows with the aid of pneumoperitoneum or by indirect demonstration with the aid of a contrast medium. For the diagnosis of tuberculosis of the intestine, the authors employ not only enemas but also the oral intake of a contrast medium. They usually employ this last method first, since they were able to demonstrate the superiority of the oral over the rectal filling. The authors discuss spasticity, changes in local intestinal motility, and the so-called Stierlin symptom, in which the cecum shows lack of or incomplete filling, whereas the adjoining ileum or sections of the colon show normal filling. Peritoneal tuberculosis produces roentgenologically demonstrable changes, particularly as the result of adhesions. Patients with abdominal tuberculosis require a year or more of bed rest. It was found that such prolonged bed rest will prevent relapses. The modern chemotherapeutics are indispensable. Four different combinations were employed: (1) streptomycin and isoniazid; (2) isoniazid and thiosemicarbazone; (3) streptomycin and *p*-aminosalicylic acid; and (4) isoniazid plus *p*-aminosalicylic acid. In patients with peritoneal dissemination indicated by ascites, the authors administer streptomycin plus isoniazid for a period of from six to eight weeks, and exudation usually subsides. Streptomycin is given in daily doses of 30 mg. per kilogram of body weight and isoniazid in daily doses of from 10 to 15 mg. per kilogram of body weight. These doses did not cause damage to the eighth cranial nerve or neurological disturbances. After the administration of streptomycin is discontinued the authors replace it by thiosemicarbazone (2 mg. per kilogram of body weight). The drug treatment should be continued for six to eight months or longer. During the immediate postwar period, when effective drugs were not available, the mortality of abdominal tuberculosis reached 40%, but it has been practically zero during the last four years.

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Tuberculous Hypocorticalism. B. Besta and S. Valenti. Minerva med. **46:**1136-1141 (Oct. 27) 1955 (In Italian) [Turin, Italy].

The most common form of insufficiency of the adrenal cortex is linked with tuberculosis. This insufficiency may arise because the specific process becomes localized in the adrenals, or it may be the result of functional alteration of the adrenal cortex during the course of tuberculosis. The following classification of types of adrenocortical insufficiency that arise in tuberculous patients is suggested: (1) Addison's disease, (2) Addison-like disease, (3) functional hypocorticalism, and (4) hypophysial hypoadrenalism. In patients with Addison's disease, the Mycobacterium tuberculosis invades and destroys most of the adrenal tissue and, as a result, there is grave and almost total functional insufficiency of the gland. In Europe, this bacterium is still by far the commonest causative agent of Addison's disease (in 90% of cases). It is not difficult to diagnose frank Addison's disease. Antibacterial therapy may be useless and, in some instances, even harmful, whereas hormone substitution therapy (cortisone with desoxycorticosterone acetate and methylandrostenediol) is indicated. In the forms of Addison-like disease, the Myco. tuberculosis invades only parts of the adrenals; a good portion of the cortex parenchyma still functions, and, therefore, the insufficiency is only partial. In the cases in which laboratory tests reveal localized functional deficiencies of the adrenals, antibacterial therapy as well as hormone substitution therapy can be extremely useful. In the functional hypocorticalism that arises in the course of tuberculosis, a specific lesion of the adrenals is not evident histologically. The lipids are present in normal quantity in the fasciculated zone but are scarce in the glomerular and reticular areas. Hormonal urine assays and function tests have revealed what the authors call "functional dissociation," in that the insufficiency is marked with regard to the mineralcorticoid activity and rather slight with regard to the glycoactive function. This type of functional hypocorticalism may be responsible for some of the symptoms (asthenia, hypotension, and neurodyspeptic disorders) present in the tuberculous patient. Treatment with adrenocortical hormones may check this "dissociated hypocorticalism" and at the same time may potentiate the organic defenses and favor the action of chemotherapeutic agents and antibiotics. In hypophysial hypoadrenalism, the Myco. tuberculosis acts directly on the hypophysis and the resulting hypoadrenalism is an occult form of Simmonds' disease (hypophysial cachexia). There is no specific histological lesion of the adrenal, and the adrenocortical function is potentially unaltered. Differential diagnosis should be made between this type of hypoadrenalism and primary hypoadrenalism. This is best done by studying the adrenocortical function after prolonged stimulation with corticotropin. In the case of hypophysial hypoadrenalism, the response of the cortex to the hormone will be good. Chemotherapeutic agents, antibiotics, and hormones are indicated in the treatment of hypophysial hypoadrenalism.

Persistence of Antitoxin Levels After Tetanus-Toxoid Inoculation in Adults, and Effect of a Booster Dose After Various Intervals. J. M. Looney, G. Edsali, J. Ipsen Jr. and W. H. Chasen. New England J. Med. **254:**6-12 (Jan. 5) 1956 [Boston].

In 1949, the United States Army, Navy, and Air Force jointly adopted the procedure of administering to all their members two doses of precipitated tetanus toxoid one month apart, a third dose approximately one year later, and booster doses every four years and after injury. A similar procedure has been widely used in civilian practice since World War II. Two important questions remained unsettled: the duration of immunity after active immunization with tetanus toxoid, and how many years after the last previous dose of toxoid a subject would respond satisfactorily to a booster inoculation. A preliminary study in medical students in 1949-1950 indicated that fairly good levels of antitoxin were maintained for as long as six years after the last booster dose received during military service and that the postbooster response yielded titers generally in excess of 10 units per milliliter by three weeks after inoculation. A larger and more extended study was undertaken on 144 veterans of World War II. Tetanus-antitoxin titers were determined at intervals of one to 10 years after the last previous injection of tetanus toxoid. After the injection of booster doses of fluid or alum-precipitated toxoid, samples of blood were titrated at 6, 14, or 21 days or one year later. Antitoxin titrations showed that the levels of antitoxin were statistically identical in groups arranged according to intervals since last toxoid injection. The over-all geometric mean titer was 0.34 unit per milliliter. Thirty-five of the 144 veterans had less than 0.08 unit, and 14 had less than 0.025 unit per milliliter (the lowest value tested for). Ninety-eight of 102 subjects tested at six days after a booster dose exhibited titers above 0.08 unit per milliliter. Of the four remaining, one had no later test, one had less than 0.2 unit after 14 days and 0.025 unit after one year, and two had titers above 0.2 unit a year later (14-day samples were not done). All of 76 subjects with titers determined two or three weeks after a booster dose had levels above 0.1 unit per milliliter. All but 1 of 68 subjects tested a year after booster injection showed titers above 0.1 unit per milliliter. Ten subjects exhibited levels between 0.1 and 0.5 unit. This range may be adequate, since studies suggest that after a year has elapsed since a booster injection the subsequent drop is much slower than the fall during the first year. Of 130 subjects on whom clearly interpretable postinoculation titers were obtained, 129 were demonstrated to respond to a tetanus-toxoid booster injection. The ability to respond was unrelated to the time elapsed since the last toxoid injection. The author feels that booster doses of tetanus toxoid should be administered routinely at fairly regular intervals, and four-year intervals appear satisfactory. A routine booster at any time up to 10 years may restore immunity, and a booster dose of tetanus toxoid may be relied upon in an emergency in any fully immunized person up to 10 years after the last previous toxoid injection. In the event of multiple, extensive, or heavily contaminated injuries, especially about the head or neck, uncertainty regarding previous tetanus immunization, or delay in administering the emergency booster injection, the simultaneous administration of antitoxin and the toxoid is justified.

Treatment of Leprosy: I. Chemotherapy. J. A. Doull and R. R. Wolcott. New England J. Med. **254:**20-25 (Jan. 5) 1956 [Boston].

The authors review the treatment of leprosy with sulfones, with dihydrostreptomycin and sulfones singly and combined, with isonicotinic acid hydrazides singly and in combination with sulfones or dihydrostreptomycin, with thiosemicarbazone, with nonspecific vaccine therapy, and with cortisone and corticotropin in the complications of leprosy. The greatest advance in treatment of leprosy in recent years has been the introduction of the sulfones. These drugs, however, are neither curative nor bactericidal. They are of especial value in the healing of lepromatous ulcers, and long-continued therapy seems to assist natural processes of recovery by repressing multiplication of the bacilli. The disease apparently becomes arrested in a considerable proportion of cases. An appreciable proportion, however, relapse and may become refractory to further sulfone treatment. The Leonard Wood Memorial studies show the value of dihydrostreptomycin to be equivalent to that of the sulfones as far as can be judged after one year of therapy. Combined treatment with a sulfone and dihydrostreptomycin offers no advantage. Except for dihydrostreptomycin, the antibiotics that have been tried are of value only in treatment of secondary infections. The value of sulfone therapy in the tuberculoid type is indicated by several reports, especially that of Lowe from Nigeria, but it remains to be established by controlled studies. Tuberculoid macules may become inactive without treatment of any kind, but sensory changes remain in the residual and often depigmented scars. No method of treatment of leprosy has reversed, or can be expected to reverse, the anesthesia and trophic effects resulting from invasion of peripheral nerves by Mycobacterium leprae. This invasion occurs early in the disease, especially in the tuberculoid type. It is also an unfortunate fact that early diagnosis is the exception; frequently, the disease goes unrecognized for several years. There is therefore urgent need for educational measures directed toward earlier recognition, as well as for discovery of a drug that will have a bactericidal effect on Myco. leprae.

Physiologic Basis of Transfusion Therapy in Hemophilia. K. M. Brinkhous, G. D. Penick, R. D. Langdell and others. A. M. A. Arch. Path. **61**:6-10 (Jan.) 1956 [Chicago].

Most investigators agree that hemophilia results from the congenital deficiency of a specific plasma protein, the antihemophilic factor, that is needed for normal operation of the complex coagulation mechanism. The beneficial effect of transfusions in promoting hemostasis is dependent upon the antihemophilic factor contained in the donor plasma. This paper deals with transfusion therapy of true hemophilia, but certain of the principles outlined appear to apply likewise to at least some of the hemophilia-like states. As the result of studies in the last few years, information has been obtained on the quantitative requirements of the antihemophilic factor for the treatment of hemophilic crises. Sources of antihemophilic factor are normal plasma or plasma fractions. Normal plasma from different subjects varies widely in antihemophilic factor content. In stored bank blood or frozen plasma approximately half of the initial antihemophilic factor content is lost in two weeks. Lyophilized plasma has about one-half the potency of fresh plasma. Antihemophilic factor in reconstituted fraction 1 is about one-third of the mean normal value. Fresh plasma from selected donors appears to be the best source of antihemophilic factor currently available. The authors discuss the minimum levels of plasma antihemophilic factor required for hemostasis. Observations in man and in experimental animals have shown that a single level of a clotting factor cannot be designated as being the dividing line between adequate hemostasis and hemorrhagic diathesis. Nevertheless, several studies have indicated that there are plasma antihemophilic factor levels above which hemorrhage is unlikely to occur. The minimum hemostatic level of antihemophilic factor may be as low as 5% of normal, although some data suggest that it may be 15% to 20% of normal or higher. Of the simple laboratory tests used to follow antihemophilic factor levels after transfusions, the partial thromboplastin time and the thromboplastin generation tests appear most suitable for following antihemophilic factor changes in the critical range. The rate of loss of transfused antihemophilic factor is the third problem reviewed in this paper. The loss of antihemophilic factor after transfusion to hemophilic subjects appears to be rapid. In patients with hemophilia, the half-life of injected antihemophilic factor appears to be about four hours; in canine hemophiliacs, about two hours. These findings emphasize the need for frequent transfusions. Delayed or inadequate treatment may result in dissecting hematomas and tissue necrosis, with greatly increased requirements for antihemophilic factor.

Tuberculosis Among Nurses. J. A. Myers, R. E. Boynton and H. S. Diehl. Dis. Chest **28**:610-637 (Dec.) 1955 [Chicago].

This report is based on studies undertaken in schools of nursing since 1920. At first the studies consisted in examining and treating students who presented symptoms. Since 1927, the tuberculin test has been performed. Those who gave a positive reaction at the onset of their training period were examined semiannually while in training. Those who were uninfected (negative reactors) on entrance were retested semiannually and converters (to positive) were examined every six months. Periodic examinations of tuberculin reactors usually revealed lesions still in the silent stage, before they were contagious and when treatment was successful. Periodic testing of the uninfected provided the earliest possible diagnosis of tuberculosis. Moreover, it served as an excellent epidemiological agent. Sources of infections were sought when previously negative reactors converted to positive. This led to the discovery of such sources in affiliated hospitals, sanatoriums, and schools, and led to corrective measures. Investigation of the various protective methods for students revealed that the management of tuberculosis as a contagious disease was the only effective method. This technique was instituted in one nursing school in the early 1930's and proved so effective that it is now employed in most general hospitals in Minnesota. Periodic testing with tuberculin is the best criterion as to whether the technique is being rigidly enforced. Infection with tubercle bacilli may cause not only early illness such as pleural effusion but also and more often serious tuberculosis years and decades later. Student and graduate nurses are justified in demanding protection whenever they are in contact with contagious cases of tuberculosis. Of 5,304 nursing students who graduated from four schools of nursing in the classes from 1930 to 1954 inclusive, 807 (15.2%) had been infected before admission. Among the remaining 4,497 students, 1,020 (or 22.7%) contracted tuberculosis during training. In the classes commencing training between 1930 and 1942, over 35% of those who gave a negative tuberculin reaction on entrance converted to positive, in those between 1943 and 1949 the percentage was 17.3%, and in those after 1949, 12.1%. Those in whom the reaction to tuberculin is positive have primary lesions. Reinfection lesions developed in 26 (3.4%) of 758 students in whom positive tuberculin reactions had been obtained on entrance. Clinical tuberculosis developed later in similar percentages of those in whom the tuberculin reaction had become positive during or after the training period. Demonstrable allergic manifestations, including erythema nodosum, primary pulmonary infiltrates, and pleurisy with effusion, which appear about the time allergy is established, belong to the same category as other lesions that are too small or are not so situated as to be detectable but are present in all tuberculin reactors. They are in no way comparable to reinfection clinical lesions that evolve later. With decreased incidence of infection there has been a correspondingly reduced number of clinical lesions. Many nurses who finished training uninfected with tubercle bacilli have traveled and worked in various other parts of this country and abroad, including military service, where contagious tuberculosis is rife, but the authors have seen no evidence to substantiate the theory that those who acquired infections later in life tolerated them differently than those infected in childhood or as students. Treatment of tuberculosis among the nurses included in this study has been with the method in vogue at the time demonstrable lesions evolved. Cure seems possible with antimicrobial drugs if they are given promptly after invasion, when the lesions are small and vascular and the drugs may be expected to reach all bacilli. The tuberculin test has been the master key in this study. It detects tuberculosis earlier than any other procedure, provides evidence of effectiveness of control measures, and may determine not only when to begin but also when to stop treatment.

Symptomatology of B-Cell Adenoma of Pancreas: Report of Three Cases. A. Pedrazzini and M. Vodopivec. Schweiz. med. Wchnschr. **86**:20-23 (Jan. 7) 1956 (In German) [Basel, Switzerland].

Three cases of insuloma are described that occurred in a 42-year-old woman, a 38-year-old man, and a 38-year-old woman. Because of sudden attacks of deep unconsciousness with epileptoid convulsions and paranoid symptoms, the first patient was admitted to a sanatorium for nervous diseases, and it was there that the relationship between the comatose attacks and the patient's hypoglycemia was recognized. She then was admitted to the medical clinic of the University of Zurich, and there hyperinsulinism was detected. In the course of an attack of unconsciousness associated with excessive sweating, a blood sugar level of 12 mg. per 100 cc. was determined and the diagnosis of insuloma of the pancreas was made. On laparotomy the appearance of the pancreas was normal, but one-third of the gland was removed in an attempt to reduce the hyperinsulinism. A tumor the size of a cherry was found in the operative specimen, and microscopic examination of the tumor confirmed the diagnosis of insuloma. The patient made a complete recovery. Repeated attacks of weakness and fainting spells associated with irrational talking occurred in the man, but these could be prevented by the ingestion of sugar. The attacks became more frequent and were associated with loss of consciousness and tetaniform convulsions. In one of these attacks the patient was struck by a trolley car and hospitalized. The blood sugar level before and during these attacks was very low. Oral and intravenous administration of glucose caused only an insignificant rise, and the final values were lower than the initial values. The excretion of insulin in the urine was markedly increased. A diagnosis of primary pancreatic hyperinsulinism was made and was confirmed on laparotomy. The tail of the pancreas was removed, and microscopic examination of the tissue of the pancreas revealed an insuloma the size of a plum. The symptoms of hyper-

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insulinism subsided after the removal of the tumor. In the third patient, comatose attacks occurred when she was 28 years old in the course of her first pregnancy. A severe psychic disturbance made her admission to a sanatorium for nervous diseases necessary. The clinical aspect, constant severe hypoglycemia with blood sugar levels of 25 to 30 mg. per 100 cc. and pathological blood sugar curves revealed by dextrose and insulin-loading tests, suggested a tentative diagnosis of insuloma. The diagnosis was established after resection of the tail of the pancreas when microscopic examination revealed a tumor the size of a cherry. The findings in these three patients showed that hypoglycemia is the major clinical symptom of insuloma. The blood sugar level reaches very low values (most of these below 30 mg. per 100 cc.), and psychic disturbances may result with the onset of the first manifestations of the disease. Other valuable diagnostic methods are: (1) noting the increased body weight; (2) dextrose and insulin-loading tests: the blood sugar levels are very low, with values being lower at the end than at the start of the test; reduced sensitivity to insulin was shown by the fact that there was hardly any reaction to the administration of 10 units of insulin; the preoperative and postoperative graphic recordings of the epinephrine-loading test were not characteristic; and (3) the determination of insulin excreted in the urine. The clinical course of insuloma may be divided into an early phase, with sporadic attacks of hypoglycemia, and a late phase, with constant hypoglycemia. The spontaneous hypoglycemic crisis is interpreted as failure of the total regulation against the proliferation of B-cells.

SURGERY

Symptomatology and Surgical Treatment of Stenosis of the Aortic Isthmus: Observations on 52 Cases. E. Derra, O. Bayer and F. Loogen. Deutsche med. Wchnschr. **81:**1-4 (Jan. 6) 1956 (In German) [Stuttgart, Germany].

Of 1,000 patients with congenital cardiac and vascular defects studied by the authors at the Medical Academy of Düsseldorf, Germany, 67 had stenosis of the aortic isthmus. Subjective complaints, such as headache, cardiac sensations, and feeling of cold in the legs were not characteristic or were absent, particularly in the young patients. The difference in blood pressure between the upper and lower extremities proved to be the most important objective sign. With a rise of blood pressure in the arms, the blood pressure in the legs frequently dropped considerably, so that determination of the blood pressure could only be carried out with the aid of the oscillograph. There were similar differences between the palpable pulse in the arms and in the legs. Development of the collateral circulation was highly characteristic, and was shown in roentgenograms by markedly dilated and tortuous intercostal arteries at the lower edges of the ribs in the posterolateral region and by visible or palpable pulsations in the upper and lateral portions of the thorax. The heart was enlarged to the left, with displacement of the apex beat downward to the left. There was widening of the aortic arch. It appeared enlarged and displaced abnormally high into the upper half of the thorax. A mesosystolic, left parasternal murmur in the second or third intercostal space, frequently dorsal between the scapulas to the left of the vertebral column, proved significant. In only 50% of the patients was a typical left electrocardiogram observed, with occasional signs of damage to the muscles of the left ventricle. Roentgenologic examination proved to be of considerable aid in preoperative evaluation of the condition. Except for infants, angiocardiography from a brachial vein does not seem suitable for obtaining a satisfactory filling of the aorta with the contrast medium. The stenosis was well shown with the aid of a cardiac catheter that was introduced through the left brachial artery into the aorta. Occasionally the catheter could be pushed forward into the poststenotic portion of the aorta. An 80% solution of methylglucamine salt of 3,5-diiodo-4-pyridon-N-acetic acid (Perabrodil) or triiodomethane sulfonic acid sodium (Trioabrodil) was used as contrast medium. Fifty-two patients were operated on. An end-to-end anastomosis according to the Crafoord-Gross technique was performed in 47 patients, 18 of whom were between the ages of 4 and 15 years, 25 between the ages of 16 and 25 years, and 4 between the ages of 26 and 36 years. Five patients died, excellent or good results were obtained in 29, and fair results in 3. Three operations were considered failures, since the high blood pressure in the arms did not drop, although the blood pressure in the legs was restored to normal. A homeoplastic transplantation of the aorta was performed in one 15-year-old girl, with a satisfactory result. An end-to-side anastomosis according to Blalock-Clagett's technique was performed in three patients between the ages of 10 and 17 years, two of whom died and one of whom was not benefited. A side-to-side anastomosis according to Bernhard's technique was performed in one 15-year-old patient who died. Of the eight deaths (a mortality rate of 15.4%), five occurred among the first 10 patients operated on, in whom cotton was used as suture material. Only 3 of the 42 patients died in whom silk was used for sutures; the resulting mortality rate of 7.1% corresponds to that reported by other workers.

Primary Lymphoma of the Lung. J. C. Cooley, J. R. McDonald and O. T. Clagett. Ann. Surg. **143:**18-28 (Jan.) 1956 [Philadelphia].

Primary lymphoma of the lung seems to be a rare but bona fide lesion. Records of nine cases of primary lymphoma of the lung were found in the files of the Mayo Clinic. All nine patients were explored surgically. There were four cases of Hodgkin's disease, four of lymphosarcoma, and one of reticulum cell sarcoma. The preoperative diagnosis was bronchogenic carcinoma in eight cases and Hodgkin's disease in one. All the lungs removed were restudied, and blocks were taken from representative areas for microscopic interpretation. The physician can expect little help in preoperative diagnosis from the history, physical examination, laboratory tests, bronchoscopy, or sputum studies. He must rely on the roentgenologic findings in the chest for aid in the diagnosis, and this will usually lead him to believe that he is dealing with primary cancer of the lung or with pneumonia or lung abscess. Unfortunately, many primary lymphomas of the lung present a pneumonia-like picture, with chills, fever, cough, expectoration, loss of weight, and a roentgenologic picture of consolidation of the lung. The failure of such consolidation to clear should make one suspect a more serious process. Of the nine patients in the study, five are living and four are dead. Only one patient has thus far survived more than five years after operation, and he was treated with resection of the lesion plus prophylactic roentgen-ray therapy. On the basis of observation on these nine patients and of cases reported in the literature, the authors make the following suggestions regarding treatment: Thoracotomy should be carried out early to establish a diagnosis. Resection or removal of the involved lung should be carried out when possible, with removal of as many hilar and mediastinal nodes as is technically possible. Postoperative irradiation seems advisable, regardless of the extensiveness of the resection and irrespective of whether or not the surgeon feels that he has removed all of the tumor. Repeated radiation therapy is advised for those patients who later demonstrate recurrence or for those whose condition is deemed inoperable.

Surgical Treatment of Bullous Emphysema. H. E. Walkup and M. W. Wolcott. Dis. Chest **28:**638-650 (Dec.) 1955 [Chicago].

The term bullous emphysema is applied to the roentgenologically demonstrable air cysts that appear in patients with chronic hypertrophic emphysema. The authors differentiate two types, a localized and a generalized type. The localized type is limited to one lobe or to one or more segments or subsegments of a lobe. It should be differentiated from the generalized type of bullous emphysema, in which blebs and bullae are encountered as part of a diffuse, bilateral hypertrophic emphysema. Particularly with regard to the surgical treatment, the localized type of bullous emphysema may be regarded as a separate entity. Of the 16 patients in whom the authors performed surgical treatment, 2 had the localized type. In these two cases, the bullae were excised and the results of surgical treatment were excellent. This leaves 14 with the generalized type. Nine of the 14 showed great improvement, and four moderate improvement. Only one patient, who had a 20-year history of chronic bronchitis and who had the early signs of cor pulmonale at the time of surgery, derived no benefit from the surgical treatment.

In general, the duration of symptoms did not reflect on the ultimate improvement. While one might expect a marked disparity between results in those admitted with severe dyspnea and in those demonstrating dyspnea in a more moderate degree, the authors found that some of their most encouraging results were obtained in patients who were almost totally incapacitated by dyspnea prior to the operative procedure. Associated conditions, with the exception of chronic bronchitis, do not alter the degree of improvement. In patients with bilateral bullous formation, bilateral operation is always desirable but is not always necessary to obtain a high degree of subjective improvement. This is especially true where bilateral operation might jeopardize the life of the patient, and in such cases one should accept the results obtained on the side of maximum involvement. In the majority of cases these results are most gratifying.

Differential Section of the Spinothalamic Tract to Relieve Pain from Carcinoma of the Breast. L. A. French, G. L. Haines and W. S. Ogle. Surgery **39:**107-113 (Jan.) 1956 [St. Louis].

French and associates discuss their investigations into the problem of differential section of the spinothalamic tract to obtain relief of pain in the areas generally involved in carcinoma of the breast. These areas are the dermatomes extending from the fourth cervical level down to about the eighth thoracic level and including not only the area of the breast itself but also the adjacent areas into which cancer may spread, such as the supraclavicular region, the axilla, and the adjacent pleura. This area is not rendered analgesic with cordotomy done at the usual site, which is the second thoracic level. To obtain analgesia up to the fourth cervical level it is necessary to make the cord incision at the second cervical level. The usual section at this level results in analgesia not only over the arm and chest but also the abdomen, leg, and foot, which are areas usually not involved in carcinoma of the breast. The advantages of being able to differentially section the spinothalamic tract at the high cervical region are obvious, for this would make possible a selective analgesia of the involved areas, leaving sensation intact in the lower extremity. This investigation was undertaken in order to determine if, by differential section, a selective zone of analgesia could be established with sufficient ease and certainty to warrant more general utilization of the technique. The authors describe the results obtained in the differential section of the spinothalamic tract at the C_2 level in a series of Macaca monkeys. The second part of this investigation is concerned with the differential sectioning of the anterolateral quadrant and the testing of a series of 27 patients operated on under local anesthesia. The variability in the spinothalamic tract found by others was corroborated in these investigations. There seemed to be a reasonably consistent general pattern of location for the fibers from the specific body areas. The data culled from the first two parts of their studies were tested clinically by the purposeful differential section of the spinothalamic tract in human beings under general anesthesia. This was done in four patients with malignant neoplasms and severe intractable pain in the shoulder, arm, or upper chest. All tolerated the procedure well. There were no complications. The follow-up period ranged from 6 to 27 months. All have been free of the pain previously present.

Problem of Effectiveness of Shunt Operations (Portacaval Anastomoses) in Patients with Obstruction of Blood Flow in the Portal Vein. A. Kaufmann. Schweiz. med. Wchnschr. **86:**16-19 (Jan. 7) 1956 (In German) [Basel, Switzerland].

Two cases of postoperative occlusion of portacaval shunts are described that occurred in a 49-year-old woman with intrahepatic block and a 33-year-old woman with extrahepatic block. The first patient with advanced cirrhosis of the liver died of severe bleeding from esophageal varices five weeks after a portacaval side-to-side anastomosis had been performed. The hemorrhage probably was caused by the thrombotic occlusion of the anastomosis. Autopsy revealed a cut-like scar, 1 cm. in length, in the intima of the portal vein with a central thrombus. Microscopic examination of the narrowest area between the vena cava and the portal vein revealed coarse fibrous collagenous connective tissue embedded into the suture material. In the vena cava there was a small area of loose, rose-colored tissue with fine fibers; many lymphocytes, fibroblasts, and a few leukocytes were embedded into the mesh. The second patient, with the clinical diagnosis of extrahepatic block, old organized thrombosis of the portal vein, and hypersplenism also died of hemorrhage from perforation of an esophageal varix six weeks after side-to-side portacaval anastomosis had been performed. Autopsy revealed obliteration of the distal portion of the portal vein and the proximal portion of the vena mesenterica cranialis, and thus confirmed the presence of an old thrombosis of the portal vein that made the portacaval anastomosis ineffective. Two types of occlusion of the anastomosis thus may be distinguished according to the pathological findings: postoperative thrombosis and primary fibrous obliteration. Portal obstruction and the associated slowing of the blood flow are important causes of this not too rare complication of the shunt operation. Dysproteinemic impairment of the vascular wall causing permanent vascular dilatation may be considered as the basic condition for the occlusion of the anastomosis in patients with cirrhosis of the liver. Although portacaval anastomosis is usually indicated in patients with extrahepatic block, the author's case shows that this rule may have its exceptions.

Acute Massive Gastro-Intestinal Hemorrhage Associated with Pancreatic Heterotopic Tissue of the Stomach. J. J. Hudock, H. Wanner and C. J. Reilly. Ann. Surg. **143:**121-125 (Jan.) 1956 [Philadelphia].

The case reported is one of acute massive gastrointestinal bleeding in which heterotopic pancreatic tissue of the pylorus was found. A tentative diagnosis of bleeding peptic ulcer, ruling out esophageal varices, was made. A subtotal gastrectomy was performed. During operation the patient received 1,500 ml. of blood. He was discharged on the 12th postoperative day. He was followed for 15 months. During this time he gained 20 pounds and had no further symptoms of bleeding. Microscopic examination of the surgical specimen revealed that in the pyloric region the submucosa was greatly thickened by the presence of pancreatic tissue. Although pancreatic heterotopic tissue located in the distal stomach and the duodenum is a rare cause for acute massive gastrointestinal hemorrhage, the possibility that this can occur should be kept in mind, as operation is the indicated treatment.

On the Possibility of Prolonging Without Harm the Interruption of the Aortic Circulation by Means of Artificial Hibernation and Hypothermia. P. L. Parola, A. Bencini and G. Tiberio. Minerva cardioangiol. **3:**605-606 (Nov.) 1955 (In Italian) [Turin, Italy].

A series of experiments was carried out on dogs to ascertain whether it is possible to prolong the interruption of the arterial circulation during interventions on the descending thoracic aorta without impairing the nearby organs, especially the spinal cord. To reduce the oxygen requirements of the tissues, the authors used one of the following three methods: (1) hypothermia, which they induced either by applying a refrigerating apparatus to the body surface or by cooling the blood through extracorporeal circulation; (2) artificial hibernation, which they induced either with Laborit's method or with various pharmacological combinations; or (3) hypothermia combined with artificial hibernation. Each of these methods made it possible to interrupt the arterial circulation for long periods without apparent injury to the spinal cord. With hypothermia, either alone or combined with artificial hibernation, the arterial circulation could be interrupted for as long as one hour, whereas with artificial hibernation it could be interrupted for only 10 minutes longer than it was in control dogs that were not subjected to hibernation or hypothermia. The return to normal condition was more rapid and more definite in the dogs in which hypothermia alone had been induced than in those that had been subjected to hypothermia and artificial hibernation concurrently. The postoperative course was even less favorable in the dogs in which only artificial hibernation had been induced. This last finding is in disagreement with the theoretical concept that pharmacological protection of the organism against the onset of violent defense reactions caused by the application of cold is useful; however, more studies in this field are needed.

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Survival for More Than Five Years After Pancreatoduodenectomy for Cancers of the Ampulla and Pancreatic Head. C. Dennis and R. L. Varco. Surgery **39:**92-106 (Jan.) 1956 [St. Louis].

The authors report on two patients with cancer of the head of the pancreas who have survived more than nine years and more than six years, respectively, after resection. They also report on three patients with cancer of the ampulla of Vater who have survived more than 12, 10, and 9 years, respectively, after resection. The literature contains reports of more than 20 patients who have survived longer than five years after pancreatoduodenectomy for cancer of the ampullary region. Jaundice due to neoplastic biliary obstruction is associated with pain in more than one-third of instances. The authors no longer pay much heed to "painless jaundice" as a criterion. In the presence of deepening jaundice in patients of the cancer age group and in the absence of laboratory findings suggestive of hepatitis, study of the urobilinogen passed in feces (collected for four days), as suggested by Watson, has not misled the authors as to the carcinomatous nature of the obstruction. All of nine patients who passed less than 10 mg. of urobilinogen per day in the stool proved to have carcinomatous biliary obstruction. Establishment of the true status at the time of exploration has been facilitated by adequate exposure, freeing of the right border of the duodenum to permit inspection and palpation from behind, inspection of the hepatic artery and mesenteric vessels, and search for metastases to nodes and liver. Biopsy at the time of exploration has not been helpful and has proved dangerous because of continued pancreatic leakage when resection is not done. Biopsy material has resulted in false-negative reports. This is a situation in which the surgeon must bear the responsibility for the decision whether or not to resect. He cannot delegate it to the pathologist. The presence of localized mass without evidence of distant spread is indication for pancreatoduodenectomy. The outlook in these tumors, both pancreatic and ampullary, does not appear to be appreciably worse than the outlook in cancer of the stomach. It is likely that application to pancreatic lesions of the current vigorous approach utilized by Wangensteen in the problem of cancer of the stomach will lead to substantial improvement in that outlook.

Secondary Pancreatitis After Upper Abdominal Operations. E. Kern. Arch. klin. Chir. **281:**255-272 (No. 3) 1955 (In German) [Berlin, Germany].

Surgical intervention in the upper abdomen may occasionally be complicated by acute necrosis of the pancreas. Photometric determination of pancreatic diastase in the serum was carried out postoperatively in 66 patients who had undergone various thoracic and abdominal operations. Upper abdominal operations were performed on 52 of the 66 patients, and in 13 (21%) of these, particularly in those subjected to choledochotomy and cholecystectomy, a high postoperative increase in the serum diastase level was observed and interpreted as secondary pancreatitis. In 10 of these 11 patients the increase in enzyme had already occurred in the first postoperative hours and in some in the course of the operation. In only one patient was the maximum increase in enzyme reached after 24 hours, while in most of the others the enzyme values had been restored to normal after 24 hours. It is suggested that these severe but short reactions of the pancreas that had hitherto been frequently suspected but not confirmed depend on lesions of the distal excretory ducts of the pancreas. These lesions may be caused by intracanalicular action (probing, bougienage, surgical removal of stones), or by an injury inflicted from outside (pressure exerted by abdominal retractors, crushing, or tearing). This concept was supported by the observation that in two patients in whom the body of the pancreas itself was traumatized, the postoperative increase in the serum diastase level was not pronounced. In a patient who was operated on for severe pancreatic necrosis associated with cholangitis and cirrhosis of the liver, high serum diastase values were determined preoperatively, while immediately after the operation there was a pronounced drop in the serum diastase values, which were restored to the high preoperative level within 24 hours postoperatively. Bougienage of the papilla produced temporary improvement in the excretion, a "decompression" of the excretory ducts that lasted a few hours only. This observation supports the view that decompression of bile and pancreatic ducts is the most important procedure in the treatment of disorders of the pancreas. Although acute pancreatic necrosis did not develop in any of the 11 patients with secondary pancreatitis, the possibility of such an occurrence cannot be excluded, and consequently gentle intervention on the upper abdominal tissue is essential. An increase in serum amylase values caused by anesthetic drugs or by relaxants such as curare was observed by other workers in animal experiments, but was not confirmed by the author's studies on man.

Spigelian Hernia: Report of Four Cases. N. H. Isaacson. M. Ann. District of Columbia **25:**23-26 (Jan.) 1956 [Washington, D. C.].

The linea semilunaris or line of Spigelius is not a mere line; the blending of the muscle layers and aponeurotic sheaths is not accomplished at a sudden sharp line of demarcation, but rather over a broad zone extending a variable distance (3 to 37 mm.) from the lateral margin of the rectus. It is in this space or zone that Spigelian hernias occur. The most important etiological factor would appear to be the existence of slitlike defects in the transversalis aponeurosis along the lateral margin of the rectus muscle. Muscle-wasting, childbearing, obesity, and chronic cough are contributory causes. The majority of these hernias are quite small, and their symptoms are often obscure and the diagnosis difficult. This is especially true of a hernia that does not perforate the abdominal wall. The symptoms are aggravated by pressure, coughing, and physical exertion. Nausea, vomiting, and persistent or recurring attacks of pain may mimic a variety of gastrointestinal, biliary, renal, or pelvic disorders such as appendicitis, cholelithiasis, intestinal obstruction, ureteral colic, and salpingitis. Local pain usually occurs and increases with coughing or effort, decreasing when the hernia is reduced. The small hard mass is usually painful to touch before reduction. Reduction is often quite easy and may be accompanied by a gurgling sound or sensation. The finger may then penetrate the ring and confirm the diagnosis. While Spigelian hernias are rare, their recognition is even rarer; yet they may become important in the differential diagnosis of abdominal tumors, acute appendicitis, and intestinal obstruction. The author reports four new cases.

Intra-Arterial and Subcutaneous Oxygen in the Treatment of Peripheral Arterial Disturbances. F. Judmaier and H. A. Roedling. J. Internat. Coll. Surgeons **25:**18-25 (Jan.) 1956 [Chicago].

Four thousand intra-arterial oxygen injections were given to 235 patients with peripheral arterial disturbances. Of these, 134 had arteriosclerosis or diabetic arteriosclerosis, 81 had thromboangiitis obliterans (Buerger's disease), and 8 Raynaud's disease. In 20 patients with acute arterial embolism, embolectomy was performed first and oxygen therapy was used postoperatively; 12 patients with residual symptoms from frostbite treated by sympathetic nerve block were given oxygen subcutaneously. Intra-arterial insufflation with oxygen was carried out as follows. The oxygen, which passed from an oxygen tank through a valve to a water bottle and then into an apparatus resembling that used in pneumothorax, was injected into the femoral artery with a small-gauge needle. The displacement of the water in the bottle measured the exact amount of oxygen administered, and a manometer set in the system indicated the pressure under which the oxygen was administered. The patients were followed up for one to four years. Symptomatic relief with the intra-arterial administration of oxygen was obtained in 174 patients (74%). Twenty patients with early peripheral disease made a complete recovery. The walking tolerance of these patients was unlimited on recovery. Arterial pneumographic studies were occasionally carried out simultaneously with the therapeutic intra-arterial injection of oxygen. These studies clearly showed any alterations and the point of occlusion of the main artery; they eliminated the need of contrast studies in some cases. Arteriopneumographic studies did not reveal any information with regard to collateral vessels or the retrograde flow in the veins. Increased capillary vasodilatation was shown photomicrographically in many pa-

tients, and they were those who showed clinical or symptomatic improvement. Intramuscular or subcutaneous administration of oxygen, by which 200 to 300 cc. of oxygen was infiltrated in the extremity in such a way that it was distributed over the calf and foot, was a useful adjunct to the treatment of superficial gangrenous areas. The cost of the apparatus used for the oxygen therapy is reasonable, and with proper technique and equipment there is little risk of complications.

Pulmonary Resection in Active Cavitary (Open-Positive) Tuberculosis. R. H. Holland, J. W. Bell and E. S. Welles. J. Thoracic Surg. **31:**83-92 (Jan.) 1956 [St. Louis].

Eighty-three pulmonary resections were performed on 75 patients with persistent cavities and sputum that was positive for Mycobacterium tuberculosis. Twenty-eight patients had had drug therapy for not more than six months before admission, with no interruptions of more than two weeks. None of these patients had organisms that were resistant to chemotherapy. It was thought that 42 patients would be benefited by retreatment, and 13 showed resistant bacilli at the beginning of retreatment. At the time of operation, 19 of the 28 patients whose organisms were originally susceptible to chemotherapy still harbored susceptible organisms, but in 9 the bacilli had become completely resistant. Of the 42 patients treated again, resistant bacilli had developed in 19 by the time of the operation. Thus, a total of 32 patients who were operated on were not benefited by further chemotherapy. Despite the presence of open cavities and sputum positive for Myco. tuberculosis, excellent surgical results were obtained in the patients who could be helped by chemotherapy and only fair results in those who could not. The administration of viomycin and oxytetracycline (Terramycin) in addition to the previously used chemotherapeutic agents (streptomycin, aminosalicylic acid, and isoniazid) to nine patients with resistant organisms, started six weeks preoperatively and continued for eight weeks postoperatively, did not seem to alter the end-results. Of the three factors, open cavities, positive sputum, and bacterial resistance, the latter appears to be the most significant in regard to the postresection complications and therapeutic results. In the patient with chemotherapy-susceptible organisms who is being subjected to chemotherapy for the first time, resection should probably be performed between the third and sixth month of chemotherapy, but in the patient who has received chemotherapy before, resection should be performed several months earlier in order to avoid the development of bacterial resistance.

Lymphoma of the Lung and Pleura. W. van Hazel and R. J. Jensik. J. Thoracic Surg. **31:**19-44 (Jan.) 1956 [St. Louis].

Seven cases of pulmonary parenchymal lymphoma and five cases of pleural lymphoma are described in three men and nine women between the ages of 24 and 70 years who were admitted to two hospitals in Chicago between 1945 and 1955. Seven of the patients were under 50 years of age. Two of the patients, both in the third decade, had Hodgkin's disease, which tends to occur early in life. Of the seven patients with pulmonary lymphoma, four had silent pulmonary shadows, one had occasional blood-tinged expectoration, and two had overwhelming symptoms of toxemia, with anemia, fever, severe cough with varying degrees of productivity, and marked weight loss. Shortness of breath was the chief complaint in the patients with lymphoma of the pleura. The roentgenologic changes were extremely variable, although a circumscribed contrast density was present in four patients. In one of the patients with pleural fluid, two extrapleural densities were observed on the same side and one in the contralateral lung. Two patients had massive pulmonary involvement, and in one of these bronchial occlusion, consolidation, and abscess formation were present. In one patient with pulmonary lymphoma, disseminated nodular disease was observed in both lungs, but primarily on the right side, corresponding to the class 2 type reported by Robbins. All the patients with pleural fluid showed typical fluid shadows in their roentgenograms. Pulmonary resection with complete removal of the diseased tissues was accomplished in five patients, with survival in two of these lasting over five and one-half years and in one, one and one-third years. One patient was lost to follow-up after two years, and one died after three years from cardiac failure. Partial resection established the diagnosis in two others, allowing for adjunctive therapy with nitrogen mustard and roentgen irradiation; these two patients survived for 8½ and 13 years respectively. Pathological examination of the surgical specimens revealed that lymphocytic lymphosarcoma was the most common histological type; conditions in the patients with lesions of this type were more favorable to resection, and survival rates among these patients were the best. The prognosis of lymphoma as a whole would seem to be more favorable than that of pulmonary or pleural carcinoma.

Decortication of the Lung in Tuberculous Disease: A Study in 43 Cases. T. Savage and H. A. Fleming. Thorax **10:**293-308 (Dec.) 1955 [London, England].

Constrictive pleuritis may occur as an effect of tuberculosis or as a complication of artificial pneumothorax treatment. Once established, this condition gives rise to loss of respiratory function, to danger from an unobliterated pleural space which, if not already infected, is liable to become so, and, occasionally, to symptoms resulting from a displaced mediastinum. Frequent aspiration provides no answer; simple drainage means a permanent "tube life"; an oleothorax as a rule causes infection. Thoracoplasty may further reduce function, and, though it may apparently obliterate the pleural space, an empyema may lie quiescent under it only to discharge itself years later. Operations of the Schede type are both mutilating and function-destroying. Decortication of the lung is a most attractive form of treatment, combining a removal of the thickened pleura and empyema with an opportunity for improving the respiratory function, allowing the mediastinum to return to the normal position, and permitting resection of the diseased segments of the lung if this is indicated. The authors made studies on 43 patients in whom decortication of the lung was carried out. Pleural effusion or artificial pneumothorax each were responsible in about an equal number of cases. The patients have been followed up for from six months to four and one-half years since operation. The indications for operation included functional considerations as well as the frequent finding of a tuberculous empyema (31 cases). The use of adequate postoperative suction to secure early and complete expansion of the lung with space obliteration and the use of hyperextension plaster casts to expand the hemithorax and the lung are of great importance. There has been no death and little morbidity. Preoperative and postoperative bronchospirometry were carried out in 18 patients and maximum breathing capacity measurements and clinical assessment in most of the others. In the majority of these patients lung function has been considerably improved. The functional assessment is not usually made until one year after operation. It is concluded that in selected cases of tuberculous pleural disease, decortication of the lung is a safe and satisfactory procedure, removing infection, obliterating space, reexpanding the lung, and improving function.

Bilateral Oophorectomy and Bilateral Adrenalectomy in Treatment of Cancer of Breast. (Preliminary Report.) J. Bastos, M. Hargreave and C. de Azevedo. Gaz. méd. port. **8:**345-354 (July-Aug.) 1955 (In Portuguese) [Lisbon, Portugal].

Two cases of cancer of the breast in women of 40 and 52 years of age, respectively, who improved as a result of surgical castration and bilateral adrenalectomy are reported. A breast tumor of irregular borders, hard on palpation and causing retraction of the nipple, was observed. One of the patients had regional adenopathy. The first patient was bedridden with asthenia and severe pain in the dorsal region and in the ribs. She complained of constant moderate headache. Recently she had developed diabetes mellitus and visual disorders. Roentgen examination of the head and dorsal segment of the spine showed metastases at the base of the cranium, osteolytic metastases at the cranial vault, destruction of the sella turcica, acute osteoporosis, and neoplastic osteolysis of the 11th and 12th dorsal vertebrae. The second patient complained of severe pain in the dorsal segment of the spine, the ribs, and the chest. Roentgen examination of the spine showed osteolysis of the fifth, sixth, and seventh dorsal vertebrae. Both patients had lost weight and were in poor condition. The treatment consisted of surgical castration and bilateral adrenalectomy, which was carried on in

two stages. The first operation consisted of surgical castration and removal of one of the adrenal glands. The remaining adrenal gland was removed three weeks later. Immediately after the first operation, pain subsided, the general condition of the patients greatly improved, and the size of the metastases diminished. The visual disorders and diabetes disappeared in the first patient. In the second patient acute adrenal insufficiency followed removal of the last adrenal gland. The complication was controlled by administration of plasma transfusion, Percorten, cortisone, and norepinephrine. Large doses of cortisone were given to the patient for several days after adrenal insufficiency had been controlled. Diabetes, probably due to cortisone, developed. The disease was controlled in a few months. Follow-up roentgenograms were taken six months and two months after the operation in the first and second patients respectively. In the first patient the roentgenograms showed recalcification of metastatic lesions of the cranium, partial reconstruction of the sella turcica, and recalcification of the dorsal vertebrae. In the second patient, the roentgenograms showed recalcification of the dorsal vertebrae. The good results of bilateral adrenalectomy and surgical castration in these cases may be related to the condition of the adrenals before they were removed. Histological examination after removal showed that the glands were hyperfunctioning, with cortical hypertrophy and a hypertrophic glomerular zone.

Fatigue Fractures of the Ulna. D. L. Evans. J. Bone & Joint Surg. **37B:**618-621 (Nov.) 1955 [London, England].

Evans observed two patients with fatigue fracture of the ulna. The first patient was a 30-year-old farm laborer and the other was a 56-year-old woman cook. The author cites three previously reported cases that greatly resembled the first of his cases. These four were young persons engaged in farm work. In three cases this entailed lifting heavy loads of manure or hay on a fork and in the fourth lifting heavy sacks of oats. In three cases, though pain was present at the fracture site, the patients were able to continue working for periods up to three weeks, and in the fourth pain was so conspicuously absent that it was nine months before the patient sought medical advice. The mechanism of injury appears to have been the same in most cases, in that the position of the forearm at the time of strain was that of full supination, with the elbow flexed to about a right angle. Thus in each case the weight was taken approximately at right angles to the ulnar shaft. Fatigue fractures are rare in the upper limb. The fatigue fracture of the metatarsal is commonly called a "march" fracture. Burrows in 1948 labelled the low fibular fracture a "running" fracture and the high fibular fracture a "jump" fracture. The ulnar fatigue fracture appears to be a "lifting" fracture.

Studies on Burns: I. The Exposure Method vs. Occlusive Dressings in the Local Treatment of Experimental Burns. S. P. Holman, E. S. Shaya, F. S. Hoffmeister and M. T. Edgerton Jr. Ann. Surg. **143:**49-56 (Jan.) 1956 [Philadelphia].

The object of this study was to compare the rate of epithelialization of identical burned wounds treated with occlusive dressings or receiving "open" treatment. Sixty third-degree burns were inflicted in symmetrical pairs to the backs of young pigs. One of each pair of burns was treated with "occlusive" dressings, while the other was left open and precautions taken to maintain cleanliness and avoid trauma. Follow-up biopsies were taken, and the histology of the two groups was compared by pathologists who did not know the source of the biopsies. The ratio of epithelialization of "open" to that of "dressed" wounds was 1.8 to 1.0. For the type of burns under study, this meant an average of 21 days as compared with 39 days for complete healing of the exposed and dressed burns respectively. In this experiment, the rate of epithelialization of burned wounds treated with the "open" method was significantly more rapid and of better quality than that of burned wounds treated with occlusive pressure dressings. This work suggested that more serious attention should be given by surgeons to the advantages of light and dryness and the avoidance of heat in the care of unhealed wounds.

NEUROLOGY & PSYCHIATRY

Diagnosis and Treatment of Subdural Hemorrhage in the Very Aged. M. T. Moore. J. Am. Geriatrics Soc. **3:**984-992 (Dec.) 1955 [Baltimore].

The diagnostic criteria for subdural hematoma in the very aged are not always clear-cut, and therefore a history of trauma to the head should be searched for even though no obvious evidence of direct head injury is present. The first of the two patients reported here, an 81-year-old woman, had fallen down several steps and had struck her head in the right occipital area. Although she bled she did not lose consciousness and withheld the information from her family and physician until a week later, at which time she consulted her physician because of headache. Several days later she was hospitalized, and examination at this time revealed that weakness of the left arm had developed three days prior to admission and that during the two days preceding admission there had been deepening coma and she had not responded to painful stimuli. In view of the history of a fall, a latent period of seven days with a clear sensorium, and then a slowly disordered consciousness, it was felt that a subdural hematoma existed. A burr hole was made over the right temporal area, but no subdural hemorrhage was seen. A burr hole on the left side disclosed an extensive subdural hematoma with a well-formed membrane. When incised, a large quantity of chocolate-colored blood escaped. The remainder was aspirated and flushed out. After temporary improvement, the patient lapsed again into a semicomatose state, and several subsequent openings of the operative wounds became necessary. After one month in the hospital she was able to walk unassisted and was in full possession of her mental faculties and motor power. Since discharge she has continued to be active both mentally and physically. In the second patient, a man, aged 84, there was a frank history of head injury. Although both of these patients recovered completely without postoperative disability, the mortality among patients operated on for subdural hematoma has been reported as ranging from 23 to 35%. The use of such diagnostic aids as carotid angiography and pneumoencephalography may be hazardous, and electroencephalography may not be available or may give equivocal results. The relatively simple and innocuous procedure of exploration by means of burr holes will not only afford a diagnosis, but, after enlargement with rongeurs, will facilitate treatment by evacuation of the subdural hemorrhage. The treatment of subdural hemorrhage in the very aged requires the "total approach," which includes diagnostic awareness of the condition, the selection of appropriate surgical methods, attention to the physiological requirements of the aged as regards water and electrolytes, maintenance of nutrition orally and/or parenterally, correction of hemic imbalances, care of preexisting or complicating medical disorders, and careful watch for further bleeding, which may necessitate repeated evacuation of subdural clots.

Serpasil Treatment in Hospital for Mentally Defective Patients. E. S. Jensen. Ugeskr. læger **117:**1463-1465 (Nov. 10) 1955 (In Danish) [Copenhagen, Denmark].

Fifty-one mentally deficient patients (14 men, 27 women, and 10 children) were treated with Serpasil in the first seven months of 1955. The patients were selected according to their psychic conditions—restless, noisy, violent, aggressive, destructive, anxious, hallucinated, or unwilling to eat. Treatment was by the mouth. Small doses were usually given at the start, gradually being increased at intervals of about a week, until effect was attained. Doses were usually up to 2 mg. three times daily for adults, and never over 6 mg. daily. The maintenance dose was often somewhat less. A 14-year-old girl died during treatment after being given 3 mg. Serpasil twice daily, which was perhaps an overdosage. After that no patient was given more than 2 mg. at a time. The duration of treatment was from less than a month to seven months. Improvement appeared after three or four days at the earliest, often after one or two weeks, and in many cases not until from four to eight weeks had passed. The effect of the Serpasil was especially good in 9 patients, good in 18, and slight, doubtful, or transient in 12; in 9 patients there was no effect and in 3 the condition was perhaps aggravated.

Side-effects were on the whole slight. Although not all the patients treated benefit from Serpasil, an agent that brings about improvement in approximately 50% of the cases treated must be counted a valuable adjuvant in the pacification of mentally deficient patients.

The Electroencephalogram in Phenylpyruvic Oliogophrenia. A. Fois, C. Rosenberg and F. A. Gibbs. Electroencephalog. & Clin. Neurophysiol. **7**:569-572 (Nov.) 1955 [Montreal, Canada].

Phenylpyruvic oligophrenia has been recognized as a disease entity since 1934, when urinary excretion of phenylpyruvic acid was detected in mentally deficient patients. The authors made electroencephalographic studies on 19 patients with this disorder. The outstanding features of the electroencephalogram in patients with phenylpyruvic amentia were found to be high voltage and the wave and spike discharges that resemble those of petit mal. They were somewhat more irregular than the classical petit mal pattern, and the pattern often appeared earlier in one hemisphere than the other or was even unilateral. They were seen best during drowsiness and light sleep. Nine of the 19 patients had clinical seizures. Seizure activity was indicated in the electroencephalograms of six of these nine patients in the waking state and in all nine during sleep. Among the 10 patients without a history of clinical convulsions, seizure activity was indicated in the electroencephalogram in 2 in the waking state and 6 during sleep. Only one patient in the group without seizures had a normal waking electroencephalogram. Thus the electroencephalogram confirms the clinical observation that epileptic disorder is a common complication in phenylpyruvic amentia. The occurrence of three per second spike and wave discharges of the petit mal type in more than one-third of the present group of patients with phenylpyruvic amentia is noteworthy, because this pattern is rare in other types of symptomatic epilepsy. It suggests that there is some causal relation between the metabolic disorder that is present in phenylpyruvic amentia and the wave and spike pattern. The most consistent abnormality was a lack of well-formed sleep patterns. Biparietal humps and spindles were either absent or poorly developed. Sleep activity was profoundly disorganized. These findings suggest a pathological process with a strong epileptic component, causing a profound disturbance of both cortical and thalamic function.

Phenylpyruvic Oligophrenia: Observations on Twelve Cases. H. Schönenberg, D. Schmidt and I. Wönckhaus. Ztschr. Kinderh. **77**:363-383 (No. 4) 1955 [Berlin, Germany].

The authors present observations on 12 patients with phenylpyruvic oligophrenia in whom the diagnosis was established by the increased urinary elimination of phenylaminopropionic acid, which was demonstrated by paper chromatography. Eleven of these cases were found among 3,134 inmates of institutions for the feeble-minded. The phenylketonuria was demonstrated with the aid of Fölling's urine test. One patient with phenylketonuria was found among 2,016 children who attended schools for the mentally retarded. Thus in urinary tests on over 5,000 patients Fölling's test revealed the characteristic green coloration in 12 cases, and in each of these 12 specimens paper chromatography disclosed increased excretion of phenylaminopropionic acid. The 12 patients ranged in age from one to 52 years. There were 6 males and 6 females. Eight of the patients are idiots and four are imbecilic. Light complexion (blond hair and blue eyes) is not an essential characteristic of patients with phenylpyruvic oligophrenia; it was absent in four of the patients. Pithecoid posture, athetoid or choreiform movements, muscular rigidity, and hyperreflexia were observed in patients with phenylpyruvic oligophrenia, but the authors feel that they cannot be regarded as characteristic of the disease, since they occur also in other forms of feeble-mindedness. The same can be said of microcephaly and brachycephaly, and also of hypogenitalism. Although some patients with phenylpyruvic oligophrenia are undersized, the same is true of patients with other forms of mental deficiency. The facial expressions were average or even pleasing. It cannot be said that phenylpyruvic oligophrenia is characterized by a special phenotype. Five of the 12 patients had a history of convulsive seizures. As regards treatment, the authors believe that a diet with a restricted phenylaminopropionic acid content will be difficult, expensive, and probably impractical for prolonged use. Substitution therapy with tyrosine is difficult because large doses may prove harmful. The authors tried tyrosine substitution therapy in one of their patients, but it proved ineffective in that it neither influenced the phenylaminopropionic acid content of serum or urine nor improved the static or mental functions. The administration of large doses of vitamin C failed in two of the reported cases in which it was tried.

Protrusions of Thoracic Intervertebral Disks. K. H. Abbott and R. H. Retter. Neurology **6**:1-10 (Jan.) 1956 [Minneapolis].

The authors report on six men and four women between the ages of 22 and 61 years with thoracic intervertebral disk protrusions. Two patients had two disk protrusions each. Of the 12 protruded disks, 6 were laterally placed, 2 were centrolateral, and 4 were central. Fifty-one thoracic disk protrusions were reported in the literature up to December, 1954; all but eight of these were central or centrolateral. The patients reported on had back, shoulder, arm, chest, and abdominal pains. Some of the patients were thought to have cardiac, pulmonary, and various types of abdominal disease. The serious neurological consequences of the central and centrolateral thoracic disk protrusions were confirmed in the authors' series, again emphasizing the need for the early recognition and surgical treatment of this problem. Protrusions of the laterally placed disks in the thoracic region gave rise to symptoms similar to those of laterally placed disks in the cervical and lumbar areas, i. e., radicular pain and back pain. Duration of symptoms varied from three months to four years, and the symptoms were erroneously thought to be manifestations of visceral disease. Since the results of surgical treatment of protruding thoracic disks are as favorable as those obtained in the surgical treatment of lateral disk protrusions in the cervical and lumbar regions, early recognition and surgical attention are most desirable. Myelography proved to be a valuable aid in the differential diagnosis of the various thoracic disk protrusions as opposed to visceral disease, spinal cord tumor, and chronic back sprain. The authors used 9 cc. of iophendylate (Pantopaque) injection as the contrast medium in most of their patients. In a few cases, 18 cc. proved helpful in showing defects in the lateral thoracic areas. Analysis of the cerebrospinal fluid had no particular value in the diagnosis, although an increase in the total protein level may indicate a large protrusion, usually central or centrolateral in position, resulting in some degree of obstruction at the site of the lesion. Calcification of the intervertebral disk was not observed. Contrary to the experience of other workers, trauma played an important causative role in four patients and was a possible causative agent in another. Consequently, if the proper congenital and degenerative conditions are present, trauma may be a causative factor. Of the 10 patients operated on, 3 obtained an excellent result, 2 a good result, and 3 a fair result. One patient was a therapeutic failure, and one died of pulmonary embolism. All thoracic disk protrusions can and should be diagnosed early and treated by surgical removal as soon as the diagnosis can be made. A wide laminectomy is necessary and the dura must be opened in the surgical treatment of most central disk protrusions. Laterally placed disks can be removed through a hemilaminectomy; if the nerve appears to be severely damaged, a wide opening will be required in order to do a dorsal root rhizotomy. There is no place for conservative management of any of these lesions. If the condition is treated properly, patients with thoracic disk protrusions will benefit from surgery as much as those with disk protrusions in the cervical region.

Cervical Vertigo. G. M. S. Ryan and S. Cope. Lancet **2**:1355-1358 (Dec. 31) 1955 [London, England].

In many cases of vertigo the cause is obscure. The neck plays a larger part in the mechanism of vertigo than is generally thought. The authors encountered three types of patients with cervical vertigo. In one group, vertigo seems to be due to cervical spondylosis. The patient whose history they cite had had a minor trauma, but the injury merely acted as a trigger mechanism, the fundamental cause being the underlying cervical spondylosis. Roentgenologic examination of the cervical spine

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showed osteoarthritic changes. The second group of patients had post-tractional vertigo, and two cases are presented to illustrate this type. They had considerable spondylosis of the cervical spines, which predisposed them to further injury. There was a clear relationship between the neck traction and the vertigo, with stretching acting as the trigger mechanism. The third group of patients had post-traumatic vertigo. One of the two patients with this type of vertigo had fallen on the base of her spine and also injured the back of her head. About three weeks after this injury she was awakened in the night by a throbbing sensation in the right side of her neck; in the morning she sat up in bed, felt her head swimming, and fell to the left. This sensation, which was momentary, was accompanied by slight nausea. About 10 minutes later she "felt fine." Later, attacks of vertigo and nausea recurred, and a vague soreness persisted in her neck. During several days' bed rest she found that bending the neck produced the attacks. A plaster cast was made to hold the patient's head and neck firmly in relation to each other. Tipping the patient did not produce vertigo while the cast was worn, but, when the cast was removed and the patient tipped with her neck bending freely, there was an immediate bout of vertigo accompanied by nystagmus. Two months later, all symptoms had disappeared, and it was no longer possible to induce vertigo. Another patient with post-traumatic vertigo was relieved by wearing a collar for six weeks. In commenting on the action mechanism of cervical vertigo, the authors suggest that in the described cases interference with the tonic neck reflexes was the cause.

PEDIATRICS

Breath-Holding Spells: A Review of the Literature and Eleven Additional Cases. A. Hinman and L. B. Dickey. A. M. A. J. Dis. Child. **91**:23-33 (Jan.) 1956 [Chicago].

Breath-holding spells, defined as a temporary interruption of respiration at the end of the expiratory phase leading to mild cyanosis, unconsciousness, or convulsive seizures, were observed in five boys and six girls in the Children's Service of the Stanford University Hospitals. The age at which the children were seen ranged from 1 year to 5 years 7 months. There was only one, however, over two and one-half years of age. The age of onset of the spells ranged from 3 to 24 months, the average being a little over 10 months. The frequency of the spells varied greatly, from 8 spells in a year to as many as 10 to 15 spells a day at times. In four children the first spell occurred after a fall or injury. In one spells occurred when she was not picked up. In another child the spells began after the birth of a sibling. In all patients the spells were precipitated by fright, pain, or anger. In 8 of the 11 children, the spells, on occasion, went on to convulsive seizures. In none of the children were there any physical findings of significance, except for three who had some degree of nutritional anemia. In several cases strained interpersonal relationships within the family were obvious. In four cases there were conflicts with the child in regard to feeding, and in three cases in regard to toilet training. In three families there was frustration in regard to relatives living in the family, and in two there was marital friction. In at least two, the parents seemed to be overly demanding and strict. There was a family history of breath-holding spells in four. One child's twin had breath-holding spells, but not to the point of unconsciousness. In six of the children the spells ceased in a few months. One child was much better two years later. One was said to have become epileptic, and three were lost to follow-up. Every effort should be directed toward removing the sources of conflict, such as coercion in eating, overly strict or too early bowel and bladder training, pressure in the matter of naps and bedtime, and other premature and excessive demands on the child. Parents should be helped to understand the differences between discipline and punishment and should be given support in establishing a tolerant and consistent disciplinary regime with the emphasis placed on distraction or diversion of the child. Frequent severe breath-holding is a symptom of profound insecurity on the part of the child. His inability to experience a satisfying relationship with his parents may be the result of their own emotional disturbances or their ambivalent or negative feelings toward him. When this is the situation, work with the parents' own emotional adjustment may be necessary. Sometimes a more or less prolonged child guidance therapeutic procedure is indicated if the child's basic emotional foundations are to become adequate for later healthy development.

Myocardial Infarction Due to Calcification of the Arteries in an Infant. H. S. Traisman, N. M. Limperis and A. S. Traisman. A. M. A. J. Dis. Child. **91**:34-37 (Jan.) 1956 [Chicago].

A case of myocardial infarction caused by calcification of the coronary arteries is described in an 8-week-old baby girl. On admission to the hospital, the infant had been ill for about 40 hours, with vomiting and cough. She was cyanotic, semicomatose, and dehydrated. Respirations were 46 per minute and were shallow, labored, and irregular. The heart rate was 148 beats per minute. The liver extended 3 finger-breadths below the right costal margin. The skin was cool and clammy. Deep tendon reflexes could not be elicited. The infant did not respond to treatment with oxygen, blood transfusion, intramuscular injections of procaine penicillin, digitalis, and *l*-ephedrine. She died five and one-half hours after admission to the hospital. Autopsy and microscopic examination of the heart revealed that the lumen of the right coronary artery was markedly narrowed by numerous calcium deposits separated by fibrous septums. There was necrosis of the cardiac muscle in a few areas, with a dense infiltration of polymorphonuclear leucocytes, eosinophils, and large giant cells. Cross section of the vessels in the periaortic tissue showed calcium deposits within the wall of small arteries with characteristics identical with those of the coronary artery. Similar deposits of calcium were present in the vessels of the otherwise normal thyroid gland and adrenal medulla. Pathological calcification of the arteries such as was observed in this infant may be either dystrophic or metastatic. Dystrophic calcification is that form in which calcium is deposited in the tissues and cells that are the seat of the disease. Metastatic calcification differs in that there is no tissue injury as a precursor and calcium is mobilized from its natural place of deposit (bone). The possible causal factors of metastatic calcification, i. e., excess of vitamin D, hyperparathyroidism, destructive lesions of bones, allergy, infection, and renal lesions, were eliminated by the history and physical examinations, and, therefore, the case reported on may be categorized as one of dystrophic calcification.

Recent Experiences with Staphylococcal Infections in Childhood. L. I. Taft. M. J. Australia **2**:970-976 (Dec. 10) 1955 [Sydney, Australia].

Of 208 autopsies performed on children who died at the Royal Children's Hospital in Melbourne, Australia, in the course of 1953, 41 revealed significant infection with Micrococcus (Staphylococcus) pyogenes. Twenty-two deaths resulted from respiratory tract infection, one from tonsillectomy complicated by micrococcic enterocolitis, nine from fibrocystic disease of the pancreas associated with micrococcic bronchopneumonia, and nine from terminal pneumonia occurring in children with other debilitating incurable disease. The clinical course and the autopsy findings showed the fulminating nature of the illness, which was associated with severe toxemia, tissue necrosis, and suppuration. In some patients there was caudalward continuity of the inflammatory process from the larynx, suggesting a descending infection from the nasopharynx. In others there was evidence of tracheobronchial spread from primary micrococcic tracheobronchitis and bronchopneumonia. In still other patients, the absence of involvement of the larynx, trachea, and bronchi and the miliary distribution of lesions in the lungs and other organs supported the view of hematogenous dissemination from superficial foci of infection. In one patient an initial influenzal infection was suspected. Hospital cross infection with terminal pneumonia and fibrocystic disease of the pancreas contributed significantly to the mortality from micrococcic infection. Antibiotic-resistant micrococci are progressively increasing, particularly since the advent of large-scale use of antibiotics in treating these infections. Their occurrence in hospitals, maternity units,

and foundling homes, from which a significant number of fatal cases originated, further emphasizes the dangers of cross infection. The use of penicillin and streptomycin alone as initial chemotherapy in suspected infection with M. pyogenes in infants would no longer appear to be rational. Death occurs from toxemia and pulmonary damage in many patients before antibiotics can have any effect. Tissue necrosis and suppuration prevent the establishment of an effective local concentration of antibiotics, and pleural involvement from rupture of an abscess may cause death at a later stage. These problems have arisen with an organism that served originally as a measure of the potency of penicillin. The introduction of newer antibiotics to deal with resistant organisms has merely postponed the problem. Thus the widespread use of chlortetracycline (Aureomycin) for the treatment of micrococcic infections in the Royal Children's Hospital in Melbourne during the latter half of 1953 was associated with a drop in the percentage of sensitive strains from 90.6 to 74.

Palpable Contractile Pyloric Tumours in the Newly Born. W. S. Craig. Arch. Dis. Childhood **30:**484-492 (Dec.) 1955 [London, England].

A palpable tumor that contracts and relaxes is generally accepted as conclusive evidence of symptoms and signs suggestive of hypertrophic pyloric stenosis in infancy. The author describes observations that made him question and investigate the significance of pyloric tumors. Accidental observations on two infants in whom pyloric tumors disappeared induced him to make studies on two series of cases. The first series included 21 infants of less than 14 days of age in whom an unsatisfactory weight progress was associated with pronounced regurgitation and/or vomiting over a period of more than 48 hours. A control series consisted of 115 healthy newborn infants who showed uninterrupted progress and who did not experience feeding difficulties. Palpable contractile pyloric tumors were detected in 17 of the 21 infants in the first group and in 25 of the 115 infants in the second. Previously recorded histories of 23 infants who, after discharge from a maternity hospital, were subsequently operated on in general hospitals for pyloric stenosis were also reviewed. A palpable contractile pyloric tumor seems to be present in a proportion of newborn infants in whom there is no organic disease. It is suggested that in the absence of muscular hypertrophy the tumor is evidence of segmental spasm of the pyloric musculature, which is not necessarily to be regarded as evidence of abnormal function. Instances of spontaneously subsiding recurrent vomiting (and regurgitation) in infants in whom tumors were felt are described, and the suggestion is made that these cases are examples of pylorospasm of a degree indicative of abnormal function. It may be difficult to differentiate pylorospasm from hypertrophic pyloric stenosis in the first few days of life, but the author makes certain suggestions such as that excessive gastric secretion of mucus is suggestive of pylorospasm rather than pyloric stenosis; that vomiting due to stenosis is usually more severe than that arising from pylorospasm; that vomiting due to stenosis, although copious, is unlikely to be truly projectile; that the tumor due to hypertrophic stenosis is harder and contracts more fiercely than that found in cases of pylorospasm; that in general the infant with pylorospasm fails to progress over a period of a few days while the baby with pyloric stenosis deteriorates progressively but not necessarily with great rapidity; that peristalsis tends to be more marked in cases of true pyloric stenosis; and that symptoms due to pylorospasm settle within a few days with treatment in the form of repeated gastric lavage.

Infantile Hypertrophic Pyloric Stenosis in Parent and Child. T. McKeown and B. MacMahon. Arch. Dis. Childhood **30:**497-500 (Dec.) 1955 [London, England].

One hundred and twelve living patients in whom the diagnosis of pyloric stenosis was confirmed by operation at the Birmingham Children's Hospital in the period 1920-1934 were traced in 1955. They had 29 children, none of whom had pyloric stenosis. By combining these results with those from two reported series, the incidence of the disease in children of affected parents is estimated as 6.9%. Ten cases of pyloric stenosis in parent and child were obtained from current records of children treated at the Birmingham Children's Hospital. By inspection of records of 2,579 patients treated in hospitals in Liverpool, Manchester, Newcastle-on-Tyne, and Sheffield, two more examples of the disease in parent and child were found. In eight of the 12 families, the affected parent was the mother. When the results are combined with those of two published series, there are 33 families, in 17 of which the mother was affected. Since pyloric stenosis is much more common in males than in females it is concluded that the risk of the disease is considerably greater (at least four times) in children of affected mothers than in children of affected fathers. It is also shown that the risk of pyloric stenosis is not spread uniformly among all offspring of parents who have had the disease, but is highly localized in certain families. Among children in families in which a parent and one child have been affected, the proportion exhibiting the disease is approximately 40%. The authors feel that these results are inconsistent with a simple genetic hypothesis and are more plausibly attributed to the influence of the early postnatal environment.

UROLOGY

Hemolysis and Transurethral Resection: A Review. C. D. Creevy. Surgery **39:**180-188 (Jan.) 1956 [St. Louis].

The free hemoglobin of the plasma was measured before and after 106 consecutive transurethral resections, with distilled water as the irrigating fluid. The maximum preoperative level was 28 mg. per 100 cc., but postoperatively it rose as high as 490, with an average of 42 mg. per 100 cc. above the preoperative figure. To make sure that this rise did not result from some factor other than the nature and absorption of the irrigating fluid, the free hemoglobin of the plasma was measured before and after (1) neurosurgical operations with surgical diathermy, (2) a variety of abdominal operations, and (3) the intravenous administration of sodium chloride solution and of 5% glucose solution. There were no significant changes. Five (later four) per cent glucose solution then was used as the irrigating solution, both to ascertain whether this would prevent a rise of plasma hemoglobin and to determine whether the irrigating fluid did enter the circulation. Measurement of the free hemoglobin of the plasma before and after 185 consecutive resections with this irrigating agent disclosed no evidence of hemolysis. The blood sugar was measured before and after 63 such operations with distilled water for irrigation. It was unaltered. Similar determinations were made in 76 cases with glucose solution for irrigation; there was an average rise of 117 mg. per 100 cc., with a maximum level of 1,079. It was apparent that, in this patient, at least a liter of fluid had entered the circulation. Since the adoption of nonhemolytic irrigating solutions in 1946, the author and his colleagues have performed transurethral prostatic resection in 2,492 consecutive patients with 24 deaths, an over-all surgical mortality of 0.96%. The syndrome of cyanosis, torpor, anemia, oliguria, jaundice, and uremia has not been seen during this time. Since the mortality before 1946 ranged from 3 to 4%, the reduction must be attributed to elimination of hemolytic reactions. Since 1947, at least 25 authors have verified the occurrence of hemolysis during transurethral prostatic resection, and most of them have accepted the value of isotonic irrigating solutions.

Carcinoma of the Prostate Gland: 5-Year Survival Following Antiandrogenic Treatment. E. J. Ganem. J. Urol. **74:**804-808 (Dec.) 1955 [Baltimore].

Ganem investigated the clinical records of 221 patients with advanced prostatic carcinoma who were treated between 1941 and 1950 by bilateral orchiectomy and estrogens or estrogens alone. Special attention was paid to the following points: rectal examination, particularly with reference to the prostate gland; serum acid phosphatase level; the condition of the upper urinary tracts as established by pyelography; the presence or absence of bone metastasis; and duration of survival. A five-year follow-up

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was obtained in all but four patients. It was found that when a patient with local malignant disease of the prostate that is too extensive for radical prostatectomy has a normal upper urinary tract as determined by excretory urography, a normal serum acid phosphatase level, and no demonstrable bone metastases, he has a 59% chance of living five years if he is treated with orchiectomy and Stilbestrol and if his vesical neck obstruction is relieved by transurethral resection, provided he survives intercurrent disease. If such a patient has hydronephrosis or elevated serum acid phosphatase level without demonstrable bone metastases and is treated in the same manner, his chance for a five-year survival falls to about 31 or 32%. If in addition to hydronephrosis and an elevated serum acid phosphatase level he has bone metastases, his chance for five-year survival approaches zero. As far as five-year survival is concerned, orchiectomy and Stilbestrol treatment proved superior to Stilbestrol alone in the group that showed no demonstrable bone metastases. The results of this study suggest that an adequate evaluation of newer treatment methods such as use of radioactive isotopes must require precise definition of the group of patients treated in terms not only of the presence or absence of bone metastases but also of the serum acid phosphatase level and the condition of the upper urinary tract, in order to insure fair comparison with results obtained by existing antiandrogenic methods of treatment.

Investigation of Fate of Patients with Histologically Verified Carcinoma of the Prostate. C. Fabry. Ztschr. Krebsforsch. **60:** 672-681 (No. 6) 1955 (In German) [Berlin, Germany].

The author investigated the survival of 87 patients who in the course of the last seven years had undergone resection of the prostate and in whom the presence of primary carcinoma of the prostate had been established histologically. Fifty-one of the patients had died, and 22 were ill because of recurrence or metastases. Fourteen patients felt well, although the operation had not been radical and some did not receive hormone therapy. Although 7 of these 14 had been operated on within the last two and one-half years, in the other 7 up to seven years had elapsed since the operation and the establishment of the presence of cancer. Two possible explanations for this long survival are considered: 1. Carcinoma of the prostate is a particularly slow-growing tumor that may remain latent for a long time because it produces no symptoms. 2. There are two forms of carcinoma of the prostate; one form that grows very slowly and one form that grows more rapidly and may eventually develop from the slower-growing form. The author regards the second possibility as more probable, but admits that a histological differentiation of the slow-growing from the rapid-growing forms is impossible. At any rate, the histological diagnosis of cancer of the prostate is not always a "death sentence" for the patient. It is widely recognized that there is a considerable discrepancy between the morbidity and the mortality of carcinoma of the prostate. Whereas the statistics of large life insurance companies indicate that carcinoma of the prostate causes less than 4% of the cancer deaths in men, examination of the prostate in unselected series of autopsies reveals carcinoma in a much larger percentage of men, many of whom died of other causes and never had symptoms of prostatic cancer.

Congenital Unilateral Multicystic Kidney: An Entity to Be Distinguished from Polycystic Kidney Disease and Other Cystic Disorders. Harry M. Spence. J. Urol. **74:**693-706 (Dec.) 1955 [Baltimore].

Congenital unilateral multicystic kidney should be classified as a separate entity to be distinguished from polycystic kidney disease, multilocular cyst, and multiple simple cysts. This differentiation is desirable because true polycystic kidney disease is almost invariably bilateral and ultimately fatal, whereas exactly the reverse is the rule in the entity under discussion. Although the occurrence of multilocular or multiple simple renal cysts does not imply the same poor prognosis as does the polycystic variety, it seems worthwhile to classify unilateral multicystic kidney separately from these in an effort to clarify the over-all problem of renal cystic disorders. The term "unilateral multicystic kidney" was first used in 1936 by Schwartz in describing the surgical specimen removed from a 7-month-old infant diagnosed preoperatively as having either a nephroblastoma (Wilms' tumor) or a massive hydronephrosis. The striking feature of this lesion consists of replacement of the entire kidney by an irregularly lobulated mass composed of many cysts varying in size from that of a pea to that of a hen's egg, held together like a bunch of grapes by loose connective tissue. The excretory urogram reveals nonfunction on the involved side in association with a normal contralateral kidney. It is probable that a similar lesion occurs in adults. The treatment is nephrectomy and the prognosis is good. The ureter may be normal, but generally it is absent, rudimentary, or atretic. The blood supply likewise may be variable, some operators noting a vascular pedicle and others an absence thereof. The cyst walls are composed of fibrous tissue lined by a single layer of flattened or cuboid epithelial cells. Any solid tissue encountered is seen on histological section to consist of infantile renal tubular and glomerular structures interpreted as embryonal remnants that have failed to differentiate normally and unite with the excretory system. The author reviews previously reported cases and describes the histories of four new cases. Considerable confusion exists in the literature regarding the interrelationships and differences of the renal lesions in which cyst formation is a predominant feature. Part of this confusion arises from loose use of the word "polycystic" to include any disorder in which more than one cyst is present. Since the concepts of heredity, bilaterality, progression, and death are so closely associated with the term polycystic kidney, it is suggested that this designation had best be restricted to what all recognize as true polycystic disease. Similarly, more discriminating use of the terms "multilocular," "multiple simple," and "multicystic" will help to unravel the problem of the cystic kidney.

Prevention and Treatment of Thrombophlebitis and Pulmonary Embolism in Genitourinary Surgery. C. P. Mathé and E. Solomon. J. Urol. **74:**820-827 (Dec.) 1955 [Baltimore].

Thrombophlebitis, phlebothrombosis, and pulmonary embolism occur more frequently after surgical interventions on the organs of the genitourinary tract than after operations elsewhere in the body; and pulmonary embolism occurs more often after prostatic surgery than after operations on other organs of the genitourinary tract. The authors noted that there were fewer cases of fatal pulmonary embolism after kidney operations following which the foot of the patient's bed was elevated and after high ligations and radical resections of the saphenous vein in which the Trendelenburg position was used immediately after operation. They recommend for the prevention of pulmonary embolism elevation of the foot of the bed and passive and active exercises immediately after operation to assure increased venous return flow, early ambulation to maintain that flow, and antibiotic therapy and early treatment of thrombophlebitis and phlebothrombosis. These measures assure increased venous flow during the days after operation when, because of the effects of anesthesia, stress of operation, danger of hemorrhage, and general debility, the patient is unable to get out of bed. These measures eliminate blood pooling, lessen the development and propagation of the clot, and minimize the detachment of the larger fatal embolus. All patients with signs suggestive of pulmonary embolism were scrutinized for roentgenologic evidence of emboli. Care was taken to differentiate patients with emboli from those with bronchial pneumonia, pleuritis with effusion, and atelectasis. Eighteen cases of pulmonary embolism, 5 fatal and 13 nonfatal, complicated 9,005 major operations at the hospital with which the authors are connected, an incidence of 0.19%. Six cases of pulmonary embolism complicated 1,001 operations on the genitourinary tract. The preventive measures described were used in 337 patients among whom two cases of nonfatal embolism occurred. Four cases of embolism, of which two were fatal, occurred in 664 patients in whom the prophylactic measures were not carried out. In a group of older patients, two pulmonary emboli, one of which was fatal, occurred after 193 prostatic interventions in which the Trendelenburg position was not used immediately after operation; one nonfatal embolism occurred in 134 patients in whom it was used. In 382 opera-

tions on the leg veins, two nonfatal pulmonary embolisms occurred, and in these two the foot of the bed was not elevated immediately after operation; in 1,500 similar operations in which it was, only one case of embolism occurred and it was minor. Since pulmonary embolism is one of the most frequent causes of medical deaths in the aged, it cannot be expected that the recommended measures will prevent it in every case. However, they are a step in minimizing its occurrence.

RADIOLOGY

Angiography in the Evaluation of Intracranial Trauma. J. E. Lofstrom, J. E. Webster and E. S. Gurdjian. Radiology **65**:847-856 (Dec.) 1955 [Syracuse, N. Y.].

Watchful waiting and the eventual use of trephination are preferred by many surgeons in the treatment of intracranial lesions resulting from trauma. In an attempt to reduce the high rate of diagnostic errors (30 to 40%) associated with this procedure, the authors, since 1949, have resorted more and more to carotid arteriography. Approximately 1,000 patients with head injuries are seen on the neurosurgical services of three Detroit hospitals each year. About one-half of these patients present evidence of severe intracranial damage. It is in this latter group that angiography has been useful in determining the presence of intracranial hematoma, its extent, and its localization. The results on an earlier group of 30 patients established the accuracy and reliability of the method, and a total of about 500 carotid arteriograms have been obtained since then. The authors first describe the appearance of artificially produce epidural mass lesions in cadavers and correlate these with clinical findings. This comparison indicates the reliability of angiographic findings in determining localization and volume of intracranial hematoma. A history or clinical evidence of cranial trauma is not always obtainable from patients admitted to a general hospital. Trauma may be incidental to alcoholism, a cerebral vascular accident, or conditions involving stupor or coma. By utilization of cerebral angiography, the determination of the need for surgical treatment has been possible without exploration. In some patients, angiography has made it possible to establish the diagnosis of a mass lesion earlier than in the past and before the development of a critical clinical state with resultant irreversible brain changes. The authors present representative roentgenograms to demonstrate the various types and locations of intracranial hematomas. They show that carotid angiography has advantages over pneumoencephalography as well as over electroencephalography in the study of patients with cranial injuries. If preliminary angiography is not carried out numerous trephine openings may have to be made, and even then errors are possible.

Radiotherapy of the Diencephalon in Asthma. A. Jacquelin, R. Lamy, R. Serra and A. Gratay. Semaine hôp. Paris **31**:3972-3977 (Dec. 14) 1955 (In French) [Paris, France].

Irradiation of the diencephalon was used as treatment for 247 asthmatic patients over a period of four years. Complete and lasting control of the disease was obtained in 48% of the patients in the series, considerable benefit in 14%, mediocre results in 18%, and failure in 20%. No case of asthma was aggravated among the 170 patients treated in the last two years of the study. The proportion of good results (62% in all) becomes more significant when considered in the light of the following three factors: 1. The remissions or ameliorations obtained have persisted throughout the follow-up period, which has been four or five years in some instances. 2. These good or excellent results were obtained in severe, intractable cases of asthma that had not yielded to other forms of therapy. 3. It seems evident that the proportion can be increased through observance of the indications and contraindications that are now recognized. Radiotherapy is indicated in cases where there is an important psychic and neurovegetative element, cases due to exogenous allergy, and cases where there is marked eosinophilia. It is contraindicated in cases with a strong localized bronchopulmonary component, those characterized by effort dyspnea, those with hypersecretion representative of a general exudative diathesis, and cases of psychogenic asthma in which the basic conflicts have not yet been resolved.

Observations on Cancer Caused by Roentgen Irradiation. A. Beutel and F. Skopal. Strahlentherapie **98**:570-575 (No. 4) 1955 (In German) [Munich, Germany].

Beutel and Skopal report on seven patients in whom carcinoma developed in areas treated with roentgen rays. They believe that it is exceptional for irradiation cancer to develop before 20 years have elapsed since the irradiation. In their cases, incipient squamous carcinoma was present in one patient as early as 6 years after the irradiation, but the longest latent period was 33 years; in two patients it was 32 years, in one between 17 and 20 years, in another between 23 and 25 years. The authors cite Petersen's report on 17 cases of irradiation cancer, in which latent periods of from 25 to 31 years were observed. They also show that in some radiogenic cancers roentgen treatment may prove helpful. Although the cancer that was present six years after the irradiation involved originally healthy skin (irradiation after a Wertheim operation), it may generally be said that the development of irradiation cancer is rare in healthy skin. Irradiation is not always the sole cause of cancer that develops after the irradiation of skin diseases, not even if errors were made in the technique of irradiation. Other factors may be involved, and for this reason every case must be carefully analyzed for contributing causes. Radiogenic carcinoma, particularly when there is prolonged growth, may progress beyond the field of irradiation and yet spare the healthy skin by causing it to protrude.

Herpes Zoster and Roentgen Irradiation: A Contribution to the Etiology of Herpes Zoster. W. Seelentag. Strahlentherapie **98**:582-606 (No. 4) 1955 (In German) [Munich, Germany].

On the basis of observations at the Institute for Irradiation Therapy of the University of Munich, Seelentag investigated the possibility of a causal connection between roentgen irradiation and herpes zoster. Among 4,800 patients receiving irradiation therapy there were 25 with herpes zoster. In nine of these the herpes appeared after roentgen irradiation. Observations on these patients and a review of the literature convinced the author that there is no direct causal connection between roentgen irradiation and herpes zoster. Three factors are involved in the causation of herpes zoster. 1. Infection with the herpes zoster or varicella virus, for which no essential portal of entry seems to be necessary. Traumatic influences of roentgen irradiation seem to be without influence. 2. An immunobiological condition, the exact nature and significance of which is not understood and in which the importance of the patient's general condition has not been adequately investigated and the influence of roentgen irradiation, operations, and traumas has not been proved. 3. A segment localizing factor, that is, a prolonged irritation, probably resulting from cellular infiltration or an intracellular reaction, involving the sympathetic, the spinal ganglion, or a spinal root. Various factors may be responsible for this segmental irritation, such as degenerative manifestations or chronic wear on the ligamentous apparatus of the axillary region, traumas with impairment of the vertebral column, cellular infiltration or perhaps lymphatic dissemination from malignancies of the breast, or perhaps leukemic infiltrations or those caused by Hodgkin's disease. The author feels that a causal role of local damage by roentgen rays has been disproved. Other factors, however, seem to have been statistically proved, such as the increased incidence of herpes zoster in patients with breast carcinoma, Hodgkin's disease, and probably also leukemia and osteochondrosis of the vertebral column and the fact that the incidence of herpes zoster is the same in patients who have or have not received irradiation. Roentgen irradiation of the involved segment appears to be the best therapeutic method in patients in whom herpes zoster is caused by segmental infiltrations in connection with carcinomas, Hodgkin's disease, or leukemia, and there is no justification in refraining from such treatment in the erroneous belief of a causal connection between irradiation and herpes zoster.

UNIVERSITY OF MICHIGAN LIBRARIES

BOOK REVIEWS

Growth at Adolescence. By J. M. Tanner, M.D., Ph.D., D.P.M. Cloth. $6.50. Pp. 212, with 69 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, Canada, 1955.

This book organizes and summarizes an extraordinary wealth of concrete facts about the sequence of anatomic changes in pubescent boys and girls. Successive chapters deal with growth in height and weight, development of the reproductive systems, sex differences in physique arising at adolescence, the concept of physiological age, factors affecting the adolescent growth spurt, functional changes at adolescence, the endocrinology of adolescence, motor development, changes in mentality and behavior, and the adolescent growth spurt in animals. The author's skill and experience in biometry win the reader's confidence without any resort to impressive statistical jargon. An illustration of this is found in the preface, where an important distinction is made between the two ways of constructing growth curves. The course of growth in a group of people can be surmised, if the group is large and all ages are represented, by collecting a single set of measurements on each person. This "cross sectional" method, however, sometimes gives quite different results from the "longitudinal" method by which each individual of a smaller group is measured repeatedly over a period of years. It is not generally realized that averaging data can not only conceal some genuine phenomena but also generate some illusory ones. The possibility that fallacies may arise from this source has been kept in mind by the author. The chapter on endocrinology summarizes the probable sequence of events in the adrenals, hypophysis, ovaries, and testes that explain the outward manifestations of puberty. It will be of practical interest to pediatricians confronted with precocity and other disturbances of puberty. The chapter on changes in mentality and behavior is brief, and hardly gives an adequate suggestion of the problems that worry the parents of children at this stage. It does, however, give excellent references to other publications in this field. The book is well illustrated and indexed, and it should be valuable to pediatricians, physiologists, and administrators of all organizations dealing with older children.

Antimetabolites and Cancer. Edited by Cornelius P. Rhoads. Symposium presented on December 28-29, 1953, at Boston meeting of American Association for Advancement of Science. Cloth. $5.75. Pp. 312, with 50 illustrations. American Association for the Advancement of Science, 1515 Massachusetts Ave., N.W., Washington 5, D. C., 1955.

This symposium presents opinions on antimetabolites in cancer that were held in 1953; some of them have since been abandoned. The book does, however, bring together in one volume important material presented by outstanding investigators. The first paper, by Weinhouse, summarizes much of our present knowledge of metabolism in the normal and malignant cell in a clear form for those not well versed in biochemistry and thus paves the way for better comprehension of the succeeding technical papers. Most of the other papers are so technical that they are of little value to those not working directly in the field of laboratory science. This is not a criticism of the various essayists but a reflection on the embryonic state of the control of clinical cancer with antimetabolites. The only clinical paper presented is that of Burchenal, which summarizes briefly the clinical use of folic acid antagonists and 6-mercaptopurine in the treatment of leukemia. Those who have not been previously exposed to the philosophy of the editor will be amused and stimulated by his monograph "The Seeing Eye of Science," although there may be a few questions as to the originality of some observations and the validity of some conclusions. The wide range of subjects covered, including chemistry, botany, pathology, microbiology, and clinical medicine in the field of antimetabolites, applies to more than cancer and brings out many fundamentals of growth, the essential understanding of which is necessary before the basic problem of the metabolism of malignant cells can be adequately understood. This is made clear in the interesting and informative discussion. The clinician will find that the material presented in this volume is not directly applicable to the clinical treatment of cancer.

Office Procedures. By Paul Williamson, M.D. Cloth. $12.50. Pp. 412, with illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, England, 1955.

This is a practical office book that will be of interest primarily to the general practitioner and also to the student and intern. The described procedures are comparatively simple, and the book is easy to read and informative. Black and white drawings permit the reader to visualize the problem described and the method of treatment proposed with ease. A variety of fields is covered, such as otolaryngology, ophthalmology, gynecology, obstetrics, pediatrics, minor surgery, anesthesia, and physiotherapy. There are even descriptions of a small laboratory and a brief reference to roentgenography. Those who want details will have to seek books especially devoted to subjects that are covered briefly in this volume, but as a handy general reference source the reader should find this book invaluable, particularly if he recognizes its purpose and has other books to which he may refer.

Speech after Laryngectomy. By Louis M. DiCarlo, Walter W. Amster, and Gilbert R. Herer. Comparative study of breathing and speech coordinations of laryngectomized and normal subjects, and relationships between breathing and speech coordinations and articulatory errors of laryngectomized subjects to their speech intelligibility. Syracuse University, Special Education and Rehabilitation monograph series I. William M. Cruickshank, editor. This study was supported in part by control project grant No. CS-9271 from National Cancer Institute, National Institute of Health, Public Health Service. Cloth. $4. Pp. 184, with 70 illustrations. Syracuse University Press, 920 Irving Ave., Syracuse 10, N. Y., 1955.

This is a report of a comparative study of breathing and speech coordinations of laryngectomized and normal subjects. It also deals with the relationship between the breathing and speech coordinations and discusses articulatory errors of the laryngectomized subjects with reference to their speech intelligibility. Fifteen laryngectomized men between the ages of 36 and 74 (mean 59.9) years participated. The normal subjects were 15 men between the ages of 37 and 70 (mean 60.1) years. Several occupations were followed by the active and controlled groups, and some of the subjects were retired. Elaborate procedures were set up for the study. Among other tests, kymographic records of the breathing habits and tape recordings of the speaking voice of the laryngectomized men were made. Four types of pseudovoice are roughly identified as (1) pseudowhisper, (2) pharyngeal-voice, (3) esophageal-voice, and (4) gastric-voice. The authors investigated the anatomy of the throats of the patients to determine where the pseudoglottis had been developed for speaking. For example, they considered such sites as between the base of the tongue and posterior wall of the pharynx, in back of the tongue and a tightly stretched velum, at the posterior palatine arches, the constrictor muscle of the pharynx, the folds formed laterally from the musculature of the pharynx, at the hiatus of the esophagus, and at other sites. In some instances, apparently, no source could be located. Subjects who had been laryngectomized were tested for speech intelligibility and for effort required to speak. Artificial larynxes of instrumental or mechanical types were not investigated. This volume should be valuable to surgeons who make a specialty of laryngectomy. It should be especially valuable to speech therapists and to the personnel of speech and hearing rehabilitation centers. General practitioners who have patients that have been laryngectomized can learn more about postoperative and rehabilitative problems from this report. The book is amply illustrated. There is a good survey of the literature. The book has a table of contents but no index.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUERIES AND MINOR NOTES

TUBERCULIN REACTION

To the Editor:—*Due to confusion among some medical students and house staff members regarding the tuberculin test, please explain the following points: 1. Does the positive reaction to the tuberculin test indicate the presence of live tubercle bacilli in the tissues, encapsulated or not and irrespective of pathogenicity? 2. Before the use of drug therapy was it unusual to find conversion of a tuberculin reactor, even though late in life? 3. Since the use of drug therapy are there proved cases of a conversion of a previous reactor? In such a patient is it possible for the tissues to be sensitized again to the bacilli?* *J. Edmond Bryant, M.D., Evanston, Ill.*

Answer.—Many physicians are of the opinion that the tuberculin reaction indicates the presence of live tubercle bacilli in the body. The old belief, "once a reactor, always a reactor," has been disproved by observation. Evidence has accrued to show that tuberculoprotein must be present to sustain sensitivity of tissues to tuberculin. As long as such protein is being produced and liberated, the tissues retain their sensitivity. If the bacilli die, sensitivity of tissues to tuberculin wanes and disappears. Human beings and animals can be made reactors to tuberculin by introducing sufficient numbers of dead tubercle bacilli. However, such sensitivity soon disappears unless it is sustained by periodic administration of dead bacilli. Living tubercle bacilli of low virulence that die after varying periods of time after being introduced into people or animals result in the tuberculin reaction, but after the bacilli are dead the tissues revert to the nonsensitized stage. Therefore, a characteristic tuberculin reaction can be regarded as indicating the presence of live tubercle bacilli. Before the use of antimicrobial drugs, it was observed that some persons reverted from reactors to nonreactors to tuberculin, including those late in life. Apparently no extensive study on large numbers of persons has been made to determine how often this occurs from natural infection. Administration of antimicrobial drugs to persons recently infected, and therefore tuberculin reactors, has resulted in reversion to nonreactors after eight months or longer of drug administration. It has not yet been determined whether such reversion indicates that all tubercle bacilli have been destroyed or whether they have only been suppressed to such low levels that they are not multiplying and therefore tuberculoprotein is not being liberated so as to sustain sensitivity. If they are only suppressed, it is likely that, after drug administration is discontinued, they may gradually regain activity and liberate tuberculoprotein and sensitivity may again be elicited by the tuberculin test. On the other hand, if all tubercle bacilli are destroyed by drugs in the body so that sensitivity permanently vanishes, there is no reason to suspect that a later, new exogenous infection would not result in the same sensitivity of tissues as the original one.

LOW GAMMA GLOBULIN LEVEL

To the Editor:—*A 45-year-old woman, weighing 115 lb. (52.1 kg.) and measuring 5 ft. 6 in. (167.6 cm.) tall, has a low gamma globulin level. She is unusually susceptible to respiratory infections. How much gamma globulin should I give her and how often?* *M.D., South Carolina.*

Answer.—So far as known, there are no data that enable one to answer this question with precision. One dose of 2 ml. each month during the months of greatest exposure should offer adequate protection. If a respiratory infection develops in spite of this, a dose of 4 ml. at the time should be given in addition.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

LUPUS ERYTHEMATOSUS DISSEMINATUS

To the Editor:—*Is there any positive diagnosis of lupus erythematosus disseminatus during the life of the patient? Does a bone marrow puncture demonstrating the presence of large, definitely grouped eosinophils furnish an accurate diagnosis? Is Cortone or its derivatives a specified therapy? Is there any clinic or hospital in the United States that has more information and completed more research on the subject than any other? What is the course of the disease from its inception to its termination?* *Hubert B. Haywood, M.D., Raleigh, N. C.*

Answer.—Lupus erythematosus disseminatus, preferably referred to as systemic lupus erythematosus, may present cutaneous lesions that clinically and/or histopathologically are diagnostic. In the absence of cutaneous manifestations the lupus erythematosus cell phenomenon is generally accepted as diagnostic with few exceptions (Hargraves, M. M.: Systemic Lupus Erythematosus and L. E. Cell Phenomenon [Scientific Exhibit] *Postgrad. Med.* **16**:163 [Sept.] 1954). The recognition of the lupus erythematosus cell requires proper training and experience. The presence of groups of eosinophils is not of any diagnostic significance per se. Cortisone, corticotropin (ACTH), and their derivatives are definitely of ameliorative value in the treatment of systemic lupus erythematosus but are not curative. There are many universities, institutes, and hospitals in different parts of the United States that have done research work in regard to this disease. The course of the disease varies greatly and is dependent on many factors, including the severity and extent of systemic involvement. Death may ensue within a few weeks or months after the condition is first recognized or occasionally may exist for years, with remissions and exacerbations following appropriate therapy.

THYROIDECTOMY

To the Editor:—*I am on the surgical committee of a hospital staff and would like indications for thyroidectomy.*

M.D., Indiana.

Answer.—It is difficult to be didactic about indications for thyroidectomy, as there is no universal agreement on this subject among authorities in the field. Certainly most nodular goiters with hyperthyroidism should be treated by operation. Certainly large intrathoracic goiters that are causing symptoms, any goiter that is causing definite pressure symptoms, and any goiter that is large enough to be of cosmetic importance should be removed, provided that the patient's general condition is satisfactory. It is doubtful whether all multinodular goiters require operation. Most surgeons agree that it is the solitary tumor in the younger person and the enlarging tumor that should be removed and that many small multinodular goiters do not require surgical intervention.

TUBAL LIGATION

To the Editor:—*Is tubal ligation an indication for cesarean section? Suppose the patient is multiparous and has had no difficulty with previous pregnancies. What statistics are available on the safety and advisability of performing the cesarean section because the tubal ligation will be needed, or waiting and performing a postpartum tubal ligation? What is the acceptable cesarean section rate for a general hospital?*

Burdge F. Green, M.D., Stilwell, Okla.

Answer.—Tubal ligation is not an indication for cesarean section in the multigravid woman who has had no difficulty in previous pregnancies and deliveries. If sterilization is indicated it can be carried out during the first 24 hours following delivery. This extremely simple procedure can be done under local or general anesthesia through a small incision below the umbilicus with a minimum of hazard and inconvenience to the patient. Additional surgery, such as appendectomy, is contraindicated.

Statistics indicate that simple puerperal tubal ligation is less hazardous than cesarean section. It is difficult to establish the ideal cesarean section incidence for all hospitals. In the community hospital a rate of 3 or 4% is compatible with good obstetrics. Large maternity centers to which many patients with complications are referred have reported an incidence of 5% or less.

POLYHYDRAMNIOS

To the Editor:—*I will appreciate information on the prophylaxis of polyhydramnios. The patient, 22 years old, during her first pregnancy noted an abnormal enlargement of the abdomen and weight increase from fourth month on. In the seventh month she developed backache and later breathlessness due to pressure of the enlarged uterus. The doctor decided to rupture the bag of waters (yielding a bucketful), and she delivered normally after 12 hours. The child weighed nearly 4 lb. (1,814 gm.) and died after six days. She is pregnant again (three and a half months), and a specialist has advised an empirical treatment with penicillin procaine injections, 400,000 units twice daily for eight days, which is being done at present. Her general condition is good, and as yet there is no abnormal enlargement of uterus.*

H. A. Zarnegar, M.D., Teheran, Iran.

Answer.—There is no known method whereby polyhydramnios can be prevented. Many agents such as ammonium chloride, mercurial diuretics, and other diuretics have been used to no avail. It may be some comfort to know that polyhydramnios does not tend to reoccur with subsequent pregnancies. It would seem that you could expect a favorable outcome to this pregnancy and that the empirical use of penicillin is not indicated or necessary.

CESAREAN SECTIONS

To the Editor:—*What percentage of cesarean sections would be permissible in a hospital of 300 deliveries a year? Cesarean sections are becoming more prevalent than appendectomies.*

W. J. Tucker, M.D., Ashland, Wis.

Answer.—It is difficult to fix a proper incidence for cesarean section in any one institution. Large maternities to which many patients with serious complications are directed have reported an incidence of about 5% or less. Small community hospitals may do good obstetrics and maintain an incidence as low as or lower than 3%. Increasing frequency of abdominal delivery does not necessarily increase the safety of delivery for mothers and babies. Although when indicated it may be lifesaving for mother or baby, the procedure should not be regarded as an easy way out of all difficulties. In the small hospital every case history of a patient who had an abdominal delivery should be discussed at a staff meeting, for such discussions would be enlightening and tend to decrease the number of unnecessary operations.

CHRONIC RHEUMATIC FEVER

To the Editor:—*A woman 47 years of age had acute rheumatic fever more than a year ago but she is still having recurrent attacks despite many large doses of penicillin, achromycin, and sulfonamides. Her heart is not damaged, and electrocardiogram is normal. Do you have any suggestions as to how to handle this woman? She is the breadwinner and must work.*

John D. Blackburn, M.D., Thomaston, Ga.

Answer.—The differential diagnosis in a woman aged 47 between chronic rheumatic fever and some other form of arthritis, as for example, rheumatoid disease or lupus erythematosus, is difficult. If the antistreptolysin O titer is normal, the syndrome is probably not rheumatic fever. Providing the patient actually does have rheumatic fever, she should receive anti-inflammatory drugs until the erythrocyte sedimentation rate has remained normal for at least four weeks. Appropriate doses of cortisone or sodium salicylate or a combination of the two are indicated plus adequate rest. In the presence of disease activity there is no definite indication for the use of sulfonamides or antibiotics.

POLLEN ASTHMA

To the Editor:—*I am anxious to obtain information on a precipitron, an instrument that develops an electrical charge. It is installed in the inflow register of the heating system. Air is drawn from the outside and through the precipitron, thus rendering the house free of pollens. Could you tell me the value of this instrument when installed in a house for a patient who has asthma and is allergic to pollens?*

S. L. Markovits, M.D., Transcona, Manitoba, Canada.

Answer.—The electrostatic principle is the most efficient mechanism for the removal of small air-borne particles such as pollen. When the apparatus is installed centrally at the air intake the efficiency should be good. The effect on the patient will depend largely on how much time he spends in such an atmosphere. Since most of the pollen is encountered in the daytime, when he is probably at work, his relief from hay fever cannot be complete. Experience with pollen asthma indicates that, generally, air filtration for part of the day does not suffice to prevent asthma.

SUBUNGUAL HEMORRHAGE

To the Editor:—*What are the causes of small subungual hemorrhages that appear at the periphery of the nails, without any known trauma, evidence of subacute bacterial endocarditis, or other hemorrhagic tendencies?*

J. W. Stobbe, M.D., Baltimore.

Answer.—Subungual hemorrhages have been attributed to various causes, but the most common is probably trauma. Scurvy, hemophilia, blood dyscrasias, and hemangiomatosis (Rendu-Osler-Weber disease) are said to be associated with this phenomenon sometimes; also Raynaud's disease and epilepsy. One must also consider agents that may produce hemorrhage, ergot, bromides, iodides, quinine, antipyrine, salicylates, sulfonamides, sulfonal, and animal serums. Downing's book (Cutaneous Manifestations of Systemic Diseases, Publication 201, American Lecture Series, monograph in American Lectures in Dermatology, Springfield, Ill., Charles C Thomas, Publisher, 1954, p. 92) on the cutaneous manifestations of systemic disease contains a picture of subungual hemorrhage in a patient with trichinosis.

PARALYSIS FOLLOWING PENICILLIN INJECTION

To the Editor:—*In treating a 14-month-old child for upper respiratory infection with penicillin intramuscularly, a flaccid paresis appeared the next day in the leg of injection. Could the upper respiratory infection have been a nonparalytic form of poliomyelitis that was provoked to a paralytic stage by the injection? Only slight improvement in the paresis has been noted in three weeks. X-rays of hips and legs are normal. If poliomyelitis is in the area, should all intramuscular injections be avoided?*

William G. Thomas, M.D., Sycamore, Ill.

Answer.—There is a remote possibility that paralysis was "provoked" by the intramuscular injection of penicillin. However, the appearance of the paralysis within 24 hours after the injection is against such a possibility. Elective injections should be avoided during epidemics of poliomyelitis. Further information is given in an editorial in The Journal (**149:**170 [May 10] 1952).

ANTIBIOTICS IN TREATMENT OF PERITONITIS

To the Editor:—*What antibiotic or combination of antibiotics is best in the treatment of peritonitis following acute appendicitis? What combination is best for diverticulitis?*

John P. Gifford, M.D., Vero Beach, Fla.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—In the treatment of peritonitis following acute appendicitis, penicillin and streptomycin are considered the agents of choice and should be administered systemically. The addition of tetracycline is believed to add to the effectiveness of this combination. Aqueous penicillin should be administered in doses of 300,000 units every four hours and tetracycline given

intravenously in doses of 500 mg. twice daily, preferably administered in a solution of 500 cc. of dextrose (5%) and water. This regimen of therapy is also considered the method of choice in diverticulitis.

ANSWER.—A number of combinations of antibiotics have been used for the treatment of peritonitis following acute appendicitis. The writer's experience has been greatest with penicillin plus streptomycin. In about 20 cases of ruptured appendix with peritonitis, the use of 2 gm. of streptomycin plus 6 million units of aqueous crystalline benzyl penicillin G daily in divided doses for 12 to 14 days has produced recovery in all cases, with only two instances of pelvic abscess. It has been suggested that large doses of penicillin given alone are also highly effective because the important organisms to eradicate are the fecal streptococci. This consultant has greater confidence, however, in combined treatment. The same type of treatment should be successful in most instances of diverticulitis. Various combinations of "broad-spectrum" antibiotics have been used, as have neomycin and polymyxin. Because of the increased possibility of micrococcic (staphylococcic) enteritis following the use of "broad-spectrum" drugs, especially where given orally, and of serious toxic reactions that may follow the use of the other agents, this consultant prefers to start treatment with penicillin plus streptomycin. If this fails, other drugs should be employed.

NUMBNESS OF HANDS AT NIGHT

TO THE EDITOR:—*In a query in* THE JOURNAL *of Nov. 5, 1955, page 1077, the answer given to questions concerning possible causes of nocturnal paresthesias places emphasis on the scalenus anticus syndrome and neglects more important possible causes of this complaint. It would help to know whether these paresthesias are mainly in the ulnar or median parts of the hand, whether there are painful accompaniments in the shoulder or elsewhere, and, also, whether there is any blanching of the affected part or other evidences of circulatory interruption. Some people develop ulnar paresthesias during sleep, which may be due to ischemia-producing pressure on the ulnar nerve in the groove at the median epicondyle as a result of contact with the bed itself; in others the nerve is unduly mobile in its shallow groove, and, with the elbow in the flexed position, the nerve is displaced medially over the prominence of the median epicondyle, producing a symptomatic traction effect at this site. In such situations one might expect to find on questioning the patient that the paresthesias are pretty well limited to the ring and little fingers, and, on examination, one might find unusual sensitivity on percussion or palpation of the ulnar nerve in the groove; also, it might be noted that it is abnormally displaceable medially over the epicondyle by the examiner. Another type of upper extremity paresthesia is due to the effects of compression and angulation of the median nerve in the carpal tunnel beneath the transverse carpal ligament. This occurs mainly in people who sleep on one side or in a semiprone position. The wrist on the underarm may be held sharply flexed and the upper arm may be positioned so as to rest on the back of the hand, with the weight of the arm maintaining a strongly flexed position against the bed. Even though the site of abnormality is in the median nerve at the wrist, some of these individuals complain of paresthetic discomforts extending higher in the arm. Careful questioning may reveal that the principal paresthesias are centrally distributed in the hand in the median distribution, and, on examination, a strong Tinel's sign, with paresthesias in the median distribution, may be elicited on tapping over the median nerve at the transverse carpal ligament. If the examiner will hold the wrist strongly flexed for 30 to 60 seconds, he frequently can cause these paresthesias to develop while the patient is being examined. Some of these patients have benefited by sleeping at night with a rubber bath sponge in each hand for the fingers to close around, which is held in the hand by a single strip of adhesive tape wound around the sponge and the back of the hand. The placing of an object in the palm for the fingers to close around seems to forestall flexion wrist positions during sleep. The development of arm paresthesias during sleep, when the arms are kept over the head, is of course well known, and the mechanism here seems to be due to a costoclavicular compression of the brachial plexus and/or subclavian artery. Certain persons develop paresthesias from this mechanism in sleep without having the arms up over their heads, and, in these people, it is worthwhile to examine them in the position in which they sleep and search for pulse loss. Where this is a possibility, it is helpful to search with a stethoscope along the course of the subclavian artery, and one is frequently rewarded by being able to hear a loud subclavian artery bruit just below the midpoint of the clavicle when the arm is placed in the symptom-generating position. In cases where the patient habitually assumes the abduction position during sleep, it is helpful to let him tether his wrist to his pajama string by a light cord or bandage, about 18 in. in length. This permits adequate movement of the arms at a low level but does not permit them to be raised up above the shoulder. Cervical rib compression of the subclavian artery and/or the brachial plexus may become symptomatic at night. In these patients one should be able to reproduce pulse loss on assuming the symptom-producing position, and one might also hear the subclavian artery bruit located above the medial end of the clavicle. It is my belief that nocturnal paresthesias originating in compression by the scalenus anticus muscle in the absence of a cervical rib are far less frequent than the causes mentioned above.*

George Ehni, M.D.
1006 Hermann Professional Bldg.
Houston 25, Texas.

TO THE EDITOR:—*In* THE JOURNAL, *Nov. 5, page 1077, is a question on numbness of the hands at night. This is a familiar syndrome known as acroparesthesia. The description given by the inquirer is quite typical. Although more frequent in women, this is seen occasionally in men, particularly those whose occupations demand repeated flexion and extension of the wrist and the use of the butt of the hand for repeated thrusting movements. Kremer and others* (Lancet **2**:590, *1953*) *pointed out that this symptom complex was associated with compression of the median nerve beneath the transverse carpal ligament, even in the absence of objective signs referable to that nerve, and that dramatic relief follows immediately on division of this ligament. Our own experience bears this out. Prolonged rest may be effective, particularly in cases associated with pregnancy, but in the case described economic factors would prohibit this and operation ought to be undertaken. The whole transverse carpal ligament must be divided under direct vision so that a finger may be put down into the palm along the median nerve without meeting resistance.*

James Stephens, M.D.
Keasley Welch, M.D.
Divisions of Neurology and Neurosurgery
University of Colorado Medical Center
Denver.

PHENYLPYRUVIC OLIGOPHRENIA

TO THE EDITOR:—*In the Queries and Minor Notes section of* THE JOURNAL, *Jan. 7, 1956, page 88, is a question regarding the value of a phenylalanine-free diet in treatment of phenylpyruvic oligophrenia. The two consultants to whom this question was referred expressed the opinion that such a diet offered little hope of benefit for patients with this disease. On the other hand, Armstrong and Tyler of the University of Utah College of Medicine have recently published a paper on this subject in the* Journal of Clinical Investigation (**34**:565 *[April] 1955). They are extremely conservative about their interpretations, but it seems obvious from their careful studies that some benefit did result in several patients on a synthetic diet free of phenylalanine. Particularly impressive was the relief of some of the neurological symptoms. It therefore seems to me that the value of phenylalanine-free diets certainly merits additional study in the treatment of infants with phenylpyruvic oligophrenia.*

Robert J. Glaser, M.D.
Washington University
School of Medicine
St. Louis.